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It seems fitting that this first official publication of the American Society of Ophthalmologic and Otolaryngologic Allergy should be dedicated to the Founder of the organization.

And so, this volume is dedicated by the Society to

FRENCH KELLER HANSEL

AUTHOR-EDUCATOR-PHYSICIAN-SCIENTIST

Acting for the Society, and as a token of their individual affection and esteem, the Officers and Council Members of the Society have caused their signatures to be inscribed hereupon.

President

President-Elect

Vice-President

Secretary-Treasurer

Council—

FRENCH K. HANSEL, M. D., M. S.

St. Louis, Missouri

MEDICAL BIOGRAPHY

St. Louis University School of Medicine, M. D., 1918.

St. Louis City Hospital, Interne, February, 1918-February, 1919.

Missouri Baptist Hospital, Resident, February, 1919-May, 1919.

Mayo Foundation—Mayo Clinic, Fellow, May, 1919-October, 1923.

University of Minnesota and Mayo Foundation, M. S., in Otolaryngology, June, 1923; thesis on Vasomotor Rhinitis; preparation began in 1921.

Private practice in St. Louis from October, 1923.

Affiliation with Department of Otolaryngology, Washington University, October, 1923, under Dr Greenfield Sluder with Department of Allergy and Internal Medicine. Organized Allergy Clinic in Department of Otolaryngology under Dr. L. W. Dean in 1930. Associate Professor of Otolaryngology since 1930

Co-author of Hajek Diseases of the Paranasal Sinuses, 2 Vol, 1926

Fellow, American Academy of Ophthalmology and Otolaryngology, 1926.

Society of Sigma Xi, 1928

Fellow: American Laryngological, Rhinological and Otological Society, 1928

Fellow: American Academy of Allergy, 1933.

Chairman, Section on Allergy, Southern Medical Association, 1934

Author: text on *Allergy of Nose and Paranasal Sinuses, 1936.*

Fellow: American Laryngological Association, 1940, Casselbury Award for thesis on Cytology of Secretions of Nose and Paranasal Sinuses, 1940

Founder and Charter Member of American Society of Ophthalmologic and Otolaryngologic Allergy, 1941, President, 1941-1946

Charter Member and Co-organizer of American College of Allergists, 1942, President, 1944-45, Editor, Annals of Allergy, 1943-1953

Founder, Hansel Foundation, 1947, Director from 1947

Author: text on Clinical Allergy, 1953

Chief of Allergy Staff, De Paul Hospital, St Louis, Mo

Original articles and books through 1960, about 125

OFFICERS FOR 1961

Leland H. Prewitt, *President* .... Ottumwa, Iowa
Edley H. Jones, *President-Elect* .... Vicksburg, Mississippi
Lawrence S. Crispell, *Vice-President* .... Joplin, Missouri
Daniel S. De Stio, *Secretary-Treasurer* .... Pittsburgh, Pennsylvania

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Walter E. Owen .... Peoria, Illinois
Bernard M. Barrett .... Pensacola, Florida
William B. Barry .... Kansas City, Missouri
Sam H. Sanders .... Memphis, Tennessee
Francis A. O'Toole .... Clinton, Massachusetts
French K. Hansel .... St. Louis, Missouri
Frederick H. Theodore .... New York City
Michael H. Barone .... Buffalo, New York
Kenneth L. Craft .... Indianapolis, Indiana
Linden J. Wallner .... Chicago, Illinois

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Leland H. Prewitt, *President-Elect* .... Ottumwa, Iowa
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Daniel S. De Stio, *Secretary-Treasurer* .... Pittsburgh, Pennsylvania

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Kenneth L. Craft .... Indianapolis, Indiana
French K. Hansel .... St. Louis, Missouri
Francis A. O'Toole .... Clinton, Massachusetts
Sam H. Sanders .... Memphis, Tennessee
Frederick H. Theodore .... New York City

* Deceased

(Re-print St Louis Post-Dispatch, Saturday, June 5, 1948)

55 Doctors Attend School to Learn Latest on Allergies



— By a Post-Dispatch Staff Photographer

Physicians studying allergies at the Sheraton Hotel consult with DR. FRENCH K. HANSEL, standing at left. Others from left are DR. GORDON GAULTON, McGill University, Montreal, Canada, DR. DANIEL S. DE STIO, Pittsburgh, DR. L. Q. PANG, Honolulu, Hawaii, and DR. PAUL M. LEWIS, Pittsburgh, standing at right.

Course Offered for First Time by Hansel Foundation—15 Instructors Demonstrate Methods, Give Talks

Fifty-five ear, nose and throat specialists have been going to school all this week at the Sheraton Hotel, learning how to recognize and treat allergies. The course is being offered for the first time by the newly-established Hansel Foundation, named for Dr. French K. Hansel of St. Louis.

Fifteen instructors have been showing the nose and throat specialists how to make skin tests for allergies and have delivered talks on such subjects as bronchial asthma, serum disease, penicillin allergies, hay fever treatment and indications for surgery.

Chartered in February 1947, the foundation has undertaken two clinical investigations. One is an inquiry into a new hay fever treatment in which tablets of ragweed extract are used. The other is an investigation of treatment of certain types of "sinus headaches" with histamine. Both studies are still in progress but results so far were said to be encouraging.

All sections of the United States and Canada and Hawaii are represented by students in the first course, which ends tomorrow noon. There are about 8000 ear, nose and throat specialists in the United States today, the Foundation reported, "but only about 100 have adequate knowledge of allergy as related to their specialty." More than 1,000,000 children have bronchial asthma, and a "large percentage" of them are unable to obtain proper treatment, the foundation asserted.

THE AMERICAN SOCIETY OF OPHTHALMOLOGIC AND OTOLARYNGOLOGIC ALLERGY

KENNETH L. CRAFT, M.D

Indianapolis, Indiana

The origin of this Society really dates back about 25 years In 1936 Dr French K. Hansel, of St. Louis, began to give private instruction in allergy to individuals who came to his office In October of that year Dr. Hansel conducted his first class course in Nasal Allergy. This group met at Washington University and was composed of Doctors William Craddock, Monty Meyer, Lyman Richards, Charles Savery, Kinsey Simonton and Roland Starr.

Following this first group course, Dr. Hansel decided that it would be more satisfactory to conduct the instructional courses at his own office and by the year 1941 about forty otolaryngologists from all over the country had taken advantage of this opportunity to study Nasal Allergy under Dr. Hansel. This group formed the nucleus of the American Society of Ophthalmologic and Otolaryngologic Allergy which was organized during the meeting of the American Academy of Ophthalmology and Otolaryngology at Chicago in October, 1941. The stated purpose of this new organization was the "promotion of wide-spread interest in E E N T. Allergy and the dissemination of knowledge already accumulated in this subject."

The first meeting of the new Society was held at St. Louis in 1942. No further meetings were held during the course of World War 2 but the meetings were resumed in 1947 and have been held annually since that year.

The first printed program, published in 1947, carried a picture of Dr. Hansel and Stated, "This annual meeting of 1947 is dedicated to the Founder and First President of our Society, French K Hansel In order to promote further interest and progress in allergy, as related to our specialties, we believe that there is a definite need for this organization We hope that others, qualified in this special field, will join us and participate in the activities of the Society"

The first officers and council members were as follows.

President	French K Hansel
Vice-President	Wm. H Craddock
Secretary-Treasurer	W Byron Black
Council	Rea E Ashley
	L E. Darrough
	J. W. Hampsey
	Francis L. McGannon
	Walter E. Owen
	Aubrey G. Rawlins
	George E Shambaugh Jr

The first roster listed 78 active members in 1947. The meetings have been held each October during the convention of the American Academy of Ophthalmology and Otolaryngology, usually at Chicago. At the present time (1960) there are 278 Active Members and 24 Honorary Members in the Society.

Since the affairs and interests of the Society have been so closely linked with those of the Hansel Foundation, we feel that any history of the Society would be incomplete without some mention of the Foundation, the brain child of Dr. Walter E Owen, of Peoria, a Charter Member of the Society. Dr. Owen had long felt that there should be a definite, well-organized plan for the promotion of further education and research in the field of E.E.N.T. Allergy, and he suggested the establishment of a scientific foundation for this purpose to a group of the Society members at a meeting of the American Academy at Chicago in 1946. The idea caught on quickly and thus was born the Hansel Foundation, with Dr French K. Hansel as its Director. Funds were raised by means of generous contributions from Society members and from various commercial firms and other friends, and in February, 1947, a charter was granted to the new Foundation by the state of Missouri. The Hansel Foundation was incorporated under the laws of Missouri "for the diagnosis, treatment and cure of, and for medical research and study into the causes, diagnosis, treatment and cure of, ophthalmologic and otolaryngologic allergies . . ."

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President . . . . W. Byron Black

Vice-President . . . . Rea E. Ashley

Secretary-Treasurer . . . Walter E. Owen

Trustees . . . . Rea E. Ashley

W. Byron Black, Gordon J. McCurdy, F. Lambert McGannon, Walter E. Owen, Aubrey G. Rawlins, Howard L. Stitt.

Each spring since 1948 a post-graduate course in ophthalmologic and otolaryngologic allergy has been presented at St. Louis by the Foundation under the direction of Dr. Hansel and his Faculty, composed mostly of his former students. In addition to personal instruction of this type, the Foundation has conducted intensive investigation and study in a number of research projects. This has resulted in widespread dissemination of much valuable information concerning the etiology, pathology, diagnosis and treatment of allergic disease and other pathologic conditions affecting the eye, ear, nose and throat. Most of the members of the American Society of Ophthalmologic and Otolaryngologic Allergy, though not all, are former students and "Alumni" of the Hansel Foundation. Periodic reports of the workings and discoveries of the Foundation have been made available to members of the Society in Bulletins published under the direction of Dr Hansel, and financed by grants from the Society.

The rest of this History will be unfolded by listing the Past Presidents of the Society in chronological order and by giving a brief running account of incidents of interest and importance to the Society which occurred during each man's term of office. This record begins with the year 1947.



1947

FRENCH K. HANSEL, M. D

ST LOUIS

The honor which accompanies the First Presidency belongs, naturally, to the Founder of the Society. A biographical account of some of the accomplishments of Dr Hansel appears elsewhere in this journal (see p. VI)

In 1947 the Society held the first of the regular annual meetings which have continued each year to the present time The *first printed* program made its appearance at this meeting The program was published in a small attractive booklet which also carried brief histories of both the Society and the Foundation, a listing of the officers and committees of both organizations the newly adopted Constitution and By-Laws of the Society and its current roster of 78 members in that year of 1947

Features of the meeting were the excellent lecture on allergic disease given by the Guest of Honor, Mr. Reginald Ingram-Eiser, of London, England, and the presentation of an honorary key to Dr. W. Byron Black, first president of the Hansel Foundation.



1948

W. BYRON BLACK, M. D.

KANSAS CITY

On the day before this meeting was held, a refresher course in E.E.N.T. Allergy was presented by the faculty of the Foundation.

The rapid growth of the Society was indicated by the fact that the Crystal Room of the Palmer House in Chicago, where the meeting was held, was overcrowded even though the Crystal Room was four times larger than the room used the year before.

The 1948 meeting was highlighted by papers presented by three prominent Guest Speakers, Doctors M Murray Peshkin, New York, Lyman D. Richards, Brookline, Mass., and Fred W. Wittich, Minneapolis

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1949
REA E. ASHLEY, M. D.
SAN FRANCISCO

At various times, there had been proposals and attempts to bring the Society and the Foundation together into one organization. Dr. Ashley early saw the inadvisability of this move and was instrumental in pointing out the importance of preserving the autonomy of each group.

The largest attendance to date enjoyed an excellent scientific program headed by a brilliant discussion upon "Allergy in Otology" by the Guest of Honor, Professor Goste Dohlman of the University of Lund, at Lund, Sweden.



1950
GEORGE E. SHAMBAUGH, Jr. M D
CHICAGO

The first interim meeting of the Society was held at St. Louis on June 1, during the annual Course given by the Hansel Foundation. Much discussion, pro and con, was held regarding the proposal of the American Academy of Ophthalmology and Otolaryngology that the Society hold its meeting on Friday at the end of the annual Academy week, instead of prior to the Academy session. *By this move, the Academy hoped that* the Society meeting would help maintain a full attendance of Academy members until the end of its own program. As an inducement to effect this change, the Academy agreed to publish in its Transactions all of the scientific papers and discussions of the Society's programs. Action upon this matter was deferred until the regular annual meeting of the Society to be held in October, 1950.

It was proposed that the Society establish a memorial fund in honor of Dr. W. Byron Black, a charter member and Past President of the Society and a Founder of the Hansel Foundation. At the time of his death on October 23, 1949, Dr. Black was a member of the Council of the Society and was President of the Foundation. This matter also was tabled until the October meeting of the Society. At this meeting, a committee appointed to consider the matter, recommended that all funds contributed thus far be transferred to the Hansel Foundation and administered by the Trustees of the Foundation. This recommendation was adopted.

Also, at the fall meeting, it was decided that the entire Society Council should compose a committee to meet with the Council of the American Academy for discussion of the Academy's proposal regarding the meeting time of the Society.

Dr. Hansel was chosen to represent the Society at the international allergy meeting to be held at Zurich, Switzerland, in 1951

The Society's Guest of Honor this year (1950) was Herbert Rinkel, M. D., of Kansas City, who gave an excellent discussion upon "Food Allergy" Dr. Rinkel also gave a very interesting account of his recent trip to France during which he had revisited scenes of his World War I experiences. This talk was illustrated with colored slides made by Dr Rinkel and was presented at the annual banquet.



1951
WILLIAM H. EVANS, M D.
YOUNGSTOWN, OHIO

Another interim meeting was held in 1951, this time at the Edgewater Beach Hotel, Chicago, on February 11, 1951 It was decided to recommend that the Society change the time of its regular annual meeting to Friday of American Academy week

At the Society meeting held in October, 1951, the above recommendation was adopted

It was also decided to donate the sum of $2000 00 from the Society's treasury *to the W. Byron Black Memorial Fund.* This fund was to be administered by the Board of Trustees of the Hansel Foundation and was to be used to help defray the expenses of Research Fellows in the Foundation.



1952
HUGH A KUHN, M. D.
HAMMOND, INDIANA

Dr. Hansel announced plans for the publication of a Bulletin devoted to E.E.N.T Allergy, to be sent periodically to each member of the Society. It was decided to finance this project by appropriations from the treasury of the Society

The annual banquet will long be remembered for the uproarious performance of one of President Kuhn's guests, a talented magician Among other hilarious stunts, he removed Bill Owen's shirt from beneath his coat by a dexterous twist of the wrists, and then actually cut Archie Cruthirds' necktie in half when the scissors "slipped" In demonstrating this trick later with a knife, Russell Williams chopped up one of Bill Owen's gorgeous red neckties when the knife really slipped, to the delight of the audience and the discomfiture of both Owen and Williams.



1949
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Also, at the fall meeting, it was decided that the entire Society Council should compose a committee to meet with the Council of the American Academy for discussion of the Academy's proposal regarding the meeting time of the Society.



1955
F LAMBERT McGANNON, M. D.
LAKEWOOD, OHIO

The report of the Committee on Constitution and By-Laws was accepted and revisions were adopted as recommended by the Committee

Under the sponsorship of the Society, Harry B Stauffer, M D., of Jefferson City, Missouri, gave a beautifully illustrated lecture at the American Academy meeting upon "Allergic Diseases of the External Eye"



1956
DEAN M LIERLE, M D.
IOWA CITY, IOWA

Some discussion was held regarding the feasibility of changing the time of Society meetings to an earlier day of the American Academy week

A contribution from the Society of $500 00 was voted to help defray the expense of the International Congress of Otolaryngology to be held at Washington, D. C., in 1957.

Guests of Honor this year were Z. Z. Godlowski, M. D., of Northwestern University School of Medicine, T. F. Dougherty, M D., of the University of Utah College of Medicine, and J. B. Miller, M D., of Mobile, Alabama. Dr. Miller's talk upon "The Use of Mucolytic Aerosols in Respiratory Diseases" was given upon the American Academy program under the sponsorship of the Society



1957
SAM H SANDERS, M. D.
MEMPHIS, TENNESSEE

A popular improvement was added to the program booklet this year in the listing of the members geographically as well as alphabetically

In further discussion regarding a change in the time of holding the Society meetings, it was brought out that a poll of the membership showed the majority to be in favor of holding the meeting on the Saturday or Sunday just prior to the annual convention of the American Academy



1953
KENNETH L. CRAFT, M. D
INDIANAPOLIS

Plans were announced for a two-day postgraduate brush-up or refresher meeting on E.E.N.T. Allergy to be held during the annual Foundation Course at St Louis, in June, 1954.

A "Hospitality Suite," to be used as a rendezvous for Society members and friends, was maintained at the Palmer House, in Chicago, throughout the week in which the meeting was held This was to become a very popular annual feature of the Society.

The Society arranged and sponsored an excellent and beautifully illustrated lecture upon "A Study of Living Cells Taken From the Human Eye, Nose and Throat," given as a special feature of the American Academy program by Charles M. Pomerat, Ph. D., of the University of Texas School of Medicine.

It was decided that all Guest Speakers who were not Ophthalmologists nor Otolaryngologists should be made Honorary Members of the Society.

At the annual banquet, the ruckus between the North and the South was renewed by our story-telling Guest of Honor, Dr. Pomerat, and our own beloved raconteur, F. Lambert McGannon, of Cleveland. This battle of words (though *such* words) ended in a draw between the two gladiators and a victory for the delighted audience

President and Mrs. Walter Theobald and other high officials of the American Academy were guests of the Society at the banquet.



1954
ALBERT D. RUEDEMANN, M. D.
DETROIT

The meeting this year was held late in September at the Waldorf-Astoria in New York in order that our ophthalmologic members could attend the International Congress of Ophthalmology which also met in New York at the same time.

Another donation to the W. Byron Black Memorial Fund was approved at the business session. This fund was set up to provide a stipend of $200.00 per month, for a period not to exceed three months, to help defray the expenses of worthy E.E.N T. specialists for training and research work at the Hansel Foundation

A committee was appointed to revise the Constitution and By-Laws and to report its recommendations to the Society membership in time for consideration at the 1955 meeting.

changing the meeting time of the Society finally crystallized into a definite plan of action Two important decisions were made, 1) to hold the 1960 meeting on Saturday, October 8, the day before the opening of the convention of the American Academy of Ophthalmology and Otolaryngology, and 2) to devote the morning hours to the presentation of Instructional Courses in Ophthalmologic and Otolaryngologic Allergy. The overall committee consisted of Kenneth L. Craft, Indianapolis, Daniel S De Stio, Pittsburgh, French K Hansel, St. Louis, Leland H. Prewitt, Ottumwa, Iowa, Sam H Sanders, Memphis, and Walter E. Owen, Peoria, Illinois, General Chairman



1960
WALTER E OWEN, M. D
PEORIA, ILLINOIS

A three-day interim meeting was held at Saratoga, Wyoming, in July, the first of such meetings to be held at a vacation resort About twenty members, with wives and families, made the trip to Saratoga, mostly as a stop-over either while going to, or returning from, vacations in the great Northwest Round table discussions were held each morning under the leadership of Dr French Hansel, St Louis, and Dr Z Z Godlowski, Chicago. These discussions were very interesting and instructive.

Enjoyable diversions were golfing, excellent trout fishing in a branch of the Platte river, scenic side trips and just plain loafing.

Arrangements were in the capable hands of Dr. and Mrs. Russell I. Williams, of Cheyenne, Wyoming.

The fall meeting, at Chicago in October, was one of the most interesting and certainly the most unique in the history of the Society. The meeting was held at the Sherman Hotel on the Saturday just preceding the annual convention of the American Academy of Ophthalmology and Otolaryngology The morning hours were given over to an Instructional Course presented in the form of eight Round Table Conferences upon various subjects pertaining to Ophthalmologic and Otolaryngologic Allergy. Each Round Table was manned by two competent Instructors who conducted the Conferences and discussed the many questions propounded by the "students" upon various phases of allergic practice.

An equally interesting program of scientific papers was presented in the afternoon, as follows

"Repository Therapy in Allergy"—Lawrence J Halpin, M D, Cedar Rapids, Iowa

"Use of the Fluorescent Antibody Method"—Frank W Fitch, M D., Chicago.

"The Use of Cortico-Steroids in Eye, Ear, Nose and Throat Allergy"—David A. Dolowitz, M D, Salt Lake City.

"The Diagnosis and Management of Non-Granulomatous Uveitis"—Robert S Coles, M D, New York City.

Dr Coles and Dr. Dolowitz are members of the Society and Dr Fitch and



1958
JOSEPH W. HAMPSEY, M. D.
PITTSBURGH, PENNSYLVANIA

A special feature of this year's meeting was the long planned and discussed Scientific Exhibit co-sponsored by the Society and the Hansel Foundation and presented as one unit of the general scientific exhibits of the American Academy of Ophthalmology and Otolaryngology. It was planned to show the Exhibit throughout the entire Academy week but a disastrous fire broke out about midnight on Thursday in the exhibit rooms and destroyed the Society Exhibit along with several others.

It was decided that all active members of the Society to date shall be classified as "Fellows" and that hereafter all new members who are not Diplomates of either the Board of Ophthalmology or the Board of Otolaryngology shall be classified as "Associate Members", i.e., the difference between the two classes of membership shall depend upon certification by either of the above two Boards.

More and more discussion was being held concerning the Society's return to its original meeting time, i.e., on the day or two immediately preceding the American Academy session.

Distinctive cuff links bearing the seal of the Society were presented to each Past President in a fitting ceremony at the annual banquet. In the future, this award is to be presented to each President upon his retirement from office.

Another feature of the banquet was a very interesting illustrated lecture by Dr. Musil, a guest of the Society, upon his recent travels in Russia.



1959
MICHAEL H. BARONE, M. D.
BUFFALO, NEW YORK

As usual, the Society maintained its headquarters in the parlor of the Arizona Suite at the Palmer House, Chicago. Over the years, this so-called "Hospitality Suite" has proved to be just that and has been the means of welding old friendships and of making new ones as the Society members, with common interests at heart, meet each other here, year after year.

The annual program sponsored by the Society for presentation at the American Academy session consisted of a "Panel Discussion of Nasal Polyps." Members of the panel were Doctors William H. Evans, Youngstown, Ohio, French K. Hansel, St. Louis, Sam H. Sanders, Memphis, and Kenneth L. Craft, Indianapolis, Moderator.

At a post-meeting session of the Council called by incoming President Walter E. Owen, the long discussed matter of

IN MEMORIAM

			Affiliated	Died
Moore, Robert B.,	Little Rock,	Arkansas	1941	?
Norwood, Eugene P,	Waxahachie,	Texas	1941	?
James, Voyle,	Los Angeles,	California	1941	1949
Black, W Byron,	Kansas City,	Missouri	1941	1949
Fletcher, Harold A.,	San Rafael,	California	1948	1952
Mussum, William G.,	Cleveland,	Ohio	1950	1953
Gill, James P,	San Antonio,	Texas	1941	1954
Donovan, J E.,	Erie,	Pennsylvania	1953	1955
Grimmett, Roger S,	Vancouver,	British Columbia	1941	1955
Breakstone, Edgar O.,	Chicago,	Illinois	1954	1956
Harshman, Martin L,	Lafayette,	Indiana	1951	1956
Engler, Clarence W,	Cleveland,	Ohio	1949	1957
Hamilton, Richard G,	Pittsburgh,	Pennsylvania	1941	1958
Hurlbut, Jack A,	Madison,	Wisconsin	1941	1958
Kuhn, Hugh A,	Hammond,	Indiana	1941	1958
Leeson, Lavell H	Vancouver,	British Columbia	1954	1958
Stitt, Howard L,	Cincinnati,	Ohio	1941	1958
Strange, R H,	Mt. Pleasant,	Michigan	1950	1958
McGannon, F Lambert,	Lakewood,	Ohio	1941	1959
Tippen, Ernest E,	Wichita,	Kansas	1941	1959
Alvaro, Moacyr H,	San Paulo,	Brazil	1952	1960
Goodwin, Thomas M,	Elkins,	West Virginia	1954	1960
McCurdy, Gordon J,	Phoenix,	Arizona	1941	1960
Skinner, D A,	Newark,	Ohio	1949	1960

Dr. Halpin were this year's Guests of Honor.

Eighty-five members and guests attended the 1960 session and it was announced soon after the meeting was over that, due to the enthusiasm shown, and by popular request, the same type of meeting would be held in 1961. Arrangements have already been made to hold this meeting on Saturday, October 7, again at the Sherman Hotel.

PLAN NOW TO ATTEND.

(In order to avoid repetition, business matters discussed at the 1960 meeting are not mentioned here. They are, however, reported in the minutes of the meeting on another page in this volume. See page 69.)

GENERAL PRINCIPLES IN THE DIAGNOSIS AND TREATMENT OF INHALANT ALLERGY

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This paper will review, briefly, the various features of the examination and management of the patient suffering from the distressing symptoms of allergic disease of the nose and sinuses due to allergens of the inhalant class. The factors concerned in the diagnosis and treatment will be amplified in the discussions to be held at the various Conference Tables following the first two papers upon this Instructional Course program

The establishment of a diagnosis of allergic disease of the nose or sinuses may be simplified if the examining physician will follow a definite pattern of procedure in his investigation This pattern includes two main sources of information, 1) the *subjective findings* revealed by the patient, under the careful guidance of the examiner, and 2) the *objective findings* discovered by various tests and observations made by the physician himself.

SUBJECTIVE FINDINGS

The symptoms of allergic rhinitis or sinusitis include nasal blocking, spasmodic attacks of sneezing, watery or mucoid discharge, lacrimation and conjunctivitis, itching of eyes and palate, and anosmia.

A good history is the most important single factor in the diagnostic procedure. 60% to 70% of all patients suffering from nasal allergy will give a positive family history of various allergic conditions if the history is thorough and properly developed The history, then, should include the patient's ancestors and other relatives in a search for a possible hereditary allergic background of the patient's complaint A negative family history, however, does not rule out the possibility of the presence of allergy in the patient, himself

The personal history of the patient should begin with his infancy Such allergic conditions as colic, indigestion, cyclic vomiting, eczema, hives, etc., if present in early life, often will disappear spontaneously, and may be forgotten, as the child grows older. Frequently, however, these conditions are the forerunners of other types of allergy appearing in later life.

In taking the history, careful inquiry should be made as to the effect upon the symptoms of any changes in the patient's environment Has he changed his residence or his occupation? Has he bought a new mattress or rug, has he changed



tensive and chronic sinus infection.

"3. The treatment of patients with mucous polyps must include attention to the allergic factor; (the cause for the recurrence of polyps after their removal)."

The presence of nasal polyps is so significant and so pathognomonic that every case of nasal pathology demonstrating mucous polyps should be considered as allergic in origin until proven otherwise.

Cytologic examination of the nasal secretions is very important and, according to Hinnant, "is an accurate index of the pathology in the tissues" An outstanding feature in the diagnosis of nasal allergy is the demonstration of eosinophiles in stained smears of nasal secretions. Eosinophiles are prevalent in the heavier, more mucoid secretions, and are especially numerous at the height of the allergic attack

A significant feature of these cells is their tendency to group together in relatively small numbers in various areas of the field. This clumping feature is especialy diagnostic, more so, even, than the presence of a larger number of scattered individual cells. Due to various factors, these cells may not always appear at the first or even the second examination and it may be necessary to examine several stained specimens before their presence is demonstrated

Reference to the following table should be of aid in the interpretation of the various cytologic and hematologic tests used in the diagnosis of nasal disease.

1 Preponderance of EOSINOPHILES indicates ALLERGY.
2 Preponderance of NEUTROPHILES indicates INFECTION
3 Sedimentation rate of erythrocytes. increases in INFECTION but not in ALLERGY.
4. Leucopenic Index—(or digestive leukocyte response of Vaughan). In ALLERGY there is a decrease of leucocytes after the ingestion of allergenic food; (especially important in food allergy with nasal manifestations).

The cytologic and hematologic examination is extremely important in differentiating between ALLERGY and INFECTION as the causative factor in diseases of the nose and sinuses.

X-ray examination is of value in differentiating between infection and allergic disease of the sinuses. The typical x-ray picture of allergic sinusitis will show a thickened edematous lining membrane. This may vary from slight thickening of the mucosa to extreme polypoid degeneration competely filling the cavity These changes are usually confined to the antra and ethmoids. Retained secretions commonly revealed by the x-ray in purulent sinusitis are seldom seen in allergic disease unless caused by secondary infection Allergic edema involving the mucosa of the sinuses is quite transitory and the lining membrane may fluctuate considerably in size and thickening as the allergic process improves or worsens This reversible reaction may be very misleading in the interpretation of x-ray films, unless follow-up films are made at various intervals.

X-ray examination per se cannot always be relied upon in the diagnosis of sinus disease, either allergic or infectious. All rhinologists, I am sure, have had many reports from roentgenologists of positive x-ray findings in cases in which no clinical evidence of disease could be found. In allergic sinus disease the value of x-ray evidence lies in its correct in-

his diet; has a dog or other pet been introduced into the household? Has the patient, if a woman, adopted a new finger nail polish, or changed her brand of face powder or other cosmetics? Detailed information should be secured regarding the symptoms complained of; if they are constant or intermittent; if they are influenced by any of the patient's daily habits or by a vacation away from home; the effect, if any, of weather conditions and seasonal changes, or of exposure to dusts, animals, foods or other common allergens.

Many important clues leading not only to the establishment of a general diagnosis of allergy but also to the discovery of the specific cause, or allergen, responsible for the patient's complaint, may be uncovered by a good history. In history taking, the doctor should follow the pattern of a trial lawyer and cross-examine his patient in great detail in order to bring out significant points and clues which the patient may consider unimportant unless leading questions are put to him. Someone has said, very aptly, that the diagnosis of allergy is 25% science and 75% good detective work. Occasionally a case may be solved by information received in the history alone.

The classic symptoms of nasal allergy include paroxysmal attacks of sneezing, watery or mucoid nasal and lacrimal discharge, nasal obstruction, and itching of the nose, eyes and palate. Loss of taste and of the sense of smell occasionally are present in the more chronic and protracted type of case. The patient may complain of only one, or of all, of these symptoms, or of any combination of them.

OBJECTIVE EXAMINATION

In addition to the information received from the symptomatology and history, further evidence of allergic disease may be revealed by the objective findings.

Examination of the nose in a case of allergic rhinitis or sinusitis reveals a picture in sharp contrast to that seen in infection. The mucosa overlying the septum and turbinates usually will be pale and grayish white in color. Often the mucosa appears to be boggy and waterlogged in appearance, due to the presence of edema, and may be covered with a frothy mucoid secretion. Polyps and polypoid degeneration are frequently seen. Obstruction to breathing varies in degree. At times one side of the nose may be completely blocked and the other side fairly clear, and vice versa. The nasal discharge is watery or mucoid and is usually profuse, demanding frequent use of the handkerchief. Acute infection complicating allergic sinusitis may, at times, completely mask the allergic appearance of the nasal mucosa and render the diagnosis more difficult.

The presence of nasal polyps immediately suggests allergy. These growths appear much more frequently in the patient with chronic, perennial allergic disease than in the individual with the sporadic, or seasonal type. In an extensive survey of the polyp situation Kern and Schenck made the following observations:

"1. Mucous polyps are extremely common in allergic conditions of the respiratory tract.

"2. In patients with non-allergic disease of the respiratory tract mucous polyps are comparatively rare, even in the presence of ex-

should be kept as completely free from dust as possible

Special attention should be given to the toys of allergic children The fuzzy teddy bear or the wooly dog which the child likes to cuddle and take to bed should be discarded and such toys replaced by those made of wood, metal or plastics It may be necessary to get rid of pet animals or at least to deny them access to the house. They shed their hair and dander on rugs, couches and chairs and thus become a menace to many allergic individuals It would be well if "no smoking" signs could be posted and enforced in homes of smoke sensitive patients

Filter masks and inhalators afford much protection to farmers, miners, bakers, housekeepers and others who are freely exposed to irritating dusts, powders, etc Air conditioners are helpful in cleaning the air and keeping it free of irritating dusts Also of value are electric dehumidifiers, electronic dust and pollen precipitators, and filters placed in furnaces and in hot and cold air ducts The temperature of the patient's bedroom should be kept above 65°, chilling should be avoided

Chemical compounds are available as a spray for carpets, rugs, draperies, upholstered furniture, bedding, etc, and are effective in preventing the dispersion of dust from articles thus treated. One of my patients, a small boy, is sensitive to dog dander. Efforts to get rid of the child's pet dog led to such violent protest and emotional reaction that plans to banish the animal were given up. Instead, the mother periodically dunks the dog in a bucket of the chemical mentioned, and reports that the problem has been solved.

The best treatment by far, of course, for any allergic condition, is complete avoidance of contact with those allergens which are responsible for the patient's trouble. However, this cannot be accomplished with such allergens as house dust, pollens, molds, etc., which are constant inhabitants of the air which the victim must breathe For these patients, much relief may be given by hyposensitizing injections of an extract of the allergen causing the symptoms The injections are given either subcutaneously or intradermally. After the maximum amount of relief has been obtained, the dosage is held at that optimum level and is continued as a maintenance dose at the interval best suited to the patient's needs. There is no universal pattern to cover all patients' requirements; the treatment for each must be individualized

terpretation and in its correlation with the clinical and laboratory findings.

If any one of these diagnostic factors, i.e., the history, the clinical picture, the general symptoms, the laboratory examination or the x-ray findings, points to allergic involvement of the nose or sinuses, more specific etiological evidence should be sought by skin tests with the various allergens which have been suggested by the history and the clinical findings. A good history, itself, often gives the clue as to whether the offending allergen belongs in the food or in the inhalant group.

As a rule the intradermal method of skin testing is preferred. It is more sensitive and exact and gives more information than the scratch method, which usually is reserved for small children and for pollen cases.

The clinical and laboratory factors concerned in making a differential diagnosis between allergy and infection have already been mentioned. Aside from infection, allergy also must be differentiated from certain other pathologic conditions. Malnutrition, secondary anemia, hypothyroidism, etc., may produce the same color changes in the nasal mucous membrane as those caused by allergy Nasal obstruction from other causes, and certain physical agents such as gases, smoke, fumes, and temperature and climate changes, often produce nasal symptoms which may simulate an allergic attack. Psychic and emotional factors and disorders of the endocrine glands may cause nasal symptoms typical of an allergic condition, and also must be considered in the differential diagnosis.

The treatment of the inhalant form of allergic diseases of the upper respiratory tract may be considered under two main headings, 1) non-specific measures, and 2) specific therapy.

Local treatment as administered in the nose in the usual shrinking measures, has little place in allergic disease. At best, the effect is only a very temporary improvement in breathing. Recent reports from some investigators, however, indicate more prolonged and more satisfactory results from the use of steroids injected into the turbinate bodies This type of treatment has been advocated *especially in the more temporary attacks* of allergic disease, such as seasonal pollinosis

General systemic treatment is sometimes helpful and the use of certain drugs is valuable for the relief of complicating symptoms. Such drugs as ephedrine, aminophyllin, adrenalin, iodides, calcium, atropine, endocrine gland extracts (especially thyroid), sedatives, ACTH, cortisone, etc, are often of great value when indicated Antihistaminics are used extensively, probaby much more than is justified. In the inhalant type of allergic disease, these drugs are of more value in seasonal pollinosis than in perennial conditions.

Specific treatment includes, 1) prophylaxis, and 2) hyposensitization.

PROPHYLAXIS

Much can be done in a preventive way. The patient should avoid contact as much as possible, with all allergens to which he is sensitized Mattresses and pillows of dust sensitive patients should be covered with dust proof casings. Better still, sponge rubber mattresses and pillows should be substituted, if possible. Rugs, curtains, upholstered furniture and all such dust catchers and dispensers should be removed from the bedroom. The house, and especially the bedroom,

tionship between the ingestion of a specific food and the production and accentuation of allergic symptoms can be demonstrated. It does not imply positive skin reactions, nor suspected foods from the history. The main requirement of the definition is the demonstration of a cause and effect relationship between the ingestion of a food and the production of symptoms.

The generally accepted classification of food allergy is as follows:

Permanent Type In general the omission of a food leads to tolerance while frequent ingestion causes a breakdown of tolerance leading to the production of symptoms However, some foods, fortunately a small percentage, always react to produce symptoms regardless of how frequently or how infrequently they are eaten This type of food sensitivity is known as fixed or permanent.

Cyclic Type To this group belong patients who can tolerate foods they are allergic to, provided they do not eat the foods at too frequent intervals Omission of the food leads to tolerance while ingestion tends to sensitize the patient The patient goes through a cycle from the phase of tolerance to the acute phase, in which stage his symptoms are at their peak

Concomittant This is a form of food sensitization which manifests itself only when the patient is exposed to other allergenic agents to which he is sensitive, such as pollens, dust and fungi.

Thermal In this type the food sensitivity becomes manifest only when the temperature attains a critical level. The temperature levels vary with the particular area where the patient resides.

Masking Rinkel (3) describes a phenomenon to which he applies the term "masking" in which ingestion of certain foods leads to diminution or ablution of symptoms. The offending foods, while symptoms from previous ingestion are still present, are not easily detected. This situation particularly applies to foods eaten within an interval of three days or less. The phenomenon of masking is the primary reason why it is so difficult to detect offending foods.

We made an intensive study of 40 cases with proven food allergy in our practice Whereas in the literature it is implied that food allergies are most prevalent in the younger age group, we did not find this situation to prevail in our series All age groups were represented. We are seeing more cases of food sensitivities in the older age group This may be due to hormonal factors in addition to other changes in the aging individual. Sex incidence favored the female group, but we feel that the variation is too slight to be of any significance

SIGNS AND SYMPTOMS

Nasal obstruction with excessive secretion was present in all of the cases Itching of the nose and excoriation about the nares was a common finding The nasal mucous membrane appeared pale, boggy and edematous Dryness of the nose was a symptom frequenty complained of

The oropharynx presented significant symptoms Cracking at the corners of the lips was frequent The tongue was at times coated and reddened Burning of the tongue and mouth was not uncommon The mucous membrane of the

GENERAL PRINCIPLES IN THE DIAGNOSIS AND TREATMENT OF FOOD ALLERGY OF THE UPPER RESPIRATORY TRACT

SYLVESTER C. MISSAL, M. D.

Cleveland, Ohio



The significance of food allergy continues to be one of the most controversial subjects in the field of allergy. Some allergists tend to ignore it entirely; while others, notably Rowe, Rinkel, and Randolph attach considerable importance to the role food plays in the causation of symptoms. The reasons for this situation are many, chief among which are. (1) *that the cause and effect relationship* is obscure, (2) the offending food or foods are difficult to identify, and (3) the patient's full cooperation in the elimination of the harmful food from his diet is not always easy. This applies particuarly to school age children and the adult unmarried male One other important reason why the significance of food as an allergenic agent is overlooked, lies in the type of *allergic individuals* who present themselves in our offices.

We who practice otolaryngologic allergy find the problems of food allergy more acute because of the very nature of the type of allergy with which most of our *patients are affected.* The late Noah Fox of Chicago (1), a pioneer in otolaryngologic allergy referred to these patients as having borderline allergies or subclinical allergies. They are not so ill as the frank allergics who suffer from asthma, urticaria, or eczema. They come to us with the chief complaint of sinus trouble because of postnasal drip due to allergy, or nasal blockage which they blame on a broken nose, or irritation and burning of the eyes which they blame on errors of refraction; whereas the true cause *is allergy. The problem becomes* a dual one—to dissuade them from their preconceived notions as to what the cause of their trouble is, and to educate them as to the true nature of their ailment

Our interest in food allergies stemmed from the failures we encountered early in our practice of allergy some twenty years ago We concentrated all of our attention on the inhalant factors and ignored *the ingestant sensitivities because* we knew so little about them We made a study of forty such patients in our practice (2). The observations we have made materially altered our concept of the role of food allergies in the causation of ear, nose and throat symptoms.

Before going any further in our discussion, a few concepts and definitions pertaining to food allergy are in order. *Food allergy can be defined as that condition* in which a cause and effect rela-

and utilize the tests as a starting point in the therapy.

Hale (5) conceived the idea of testing with material extracted from the seeds of the fruits and vegetables for which the patient was being tested He based the rationale for the tests on the following facts:

1 The same substances are as common in the pulp as in the seeds except that the concentration is greater in the seeds

2 Experimental evidence shows that there is a common antigen in the pulp and in the seed.

3 Extracts of seeds taken as foods such as nuts and cereal grains show a relatively higher potency than do extracts of foods of which the pulp is eaten The author's point is well taken and his method may be of value in the skin testing

Skin tests are then supplemented with individual food ingestion tests as advocated by Rinkel The findings of such tests are then utilized to establish a basic diet to which foods are gradually added At times Derlacki's (6) basic diet is utilized if the patient does not do well on the original diet prescribed for him. It is not enough to instruct a patient to stay away from certain foods He must also be informed as to the sources of the harmful foods, how to avoid them and what substitute foods he can use Attention must also be taken to assure a well balanced diet with proper vitamins and minerals added.

The food allergic patients whom we see in our practice are difficult to handle Since their symptoms are not as a rule severe, many do not take the trouble to embark on a rigorous regime of food elimination and substitution such as is frequently required. Then too, the patient of today expects to be cured by "miracle drugs" and resents having to do something for himself rather than to have his physician prescribe a regime of medication which will assure a cure merely by taking pills. Many want to know why they can't go on eating the foods they like while receiving injections against foods as they do for dust or pollen. Likewise the modern day housewife has forgotten how to cook and bake. After one or two attempts at preparing a wheatless loaf of bread she gives up in despair and seeks a ready-made product at some health store where the food may be stale and unpalatable by the time it is purchased. The clinician must see the patient's side of the story and assist and encourage him as much as possible.

SUMMARY

The significance of food allergy in the practice of otolaryngology was emphasized The symptomatology, diagnosis, and treatment of food allergy was discussed The problems encountered in the handling of a food allergic patient were mentioned.

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1 Fox, N, Harned, I. W, and Peluse, S · Borderline allergy Arch of Oto., 31.502, March, 1940
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6 Derlacki, E. L.: Food sensitization as a cause of perennial nasal allergy Ann. of Allergy, 13 682, 1955

pharynx was often dull red in appearance and had at times a glossy appearance. A heavy tenacious mucous membrane film often coated the oropharynx and the nasopharynx. Islands of eosinophils could be found in stained specimens. Sore throats were frequently complained of following ingestion of the offending foods. These symptoms reached their peak in 12 to 24 hours, then gradually subsided Tenderness to palpation along the carotid vessels could often be elicited. Aphthous ulcers were not uncommon, especially in patients sensitive to cow's milk. These would disappear spontaneously when the offending foods were eliminated from the diet

Lymphadenopathy was a significant finding in some cases Patches of lymphoid hyperplasia in the mucous membrane of the pharynx and hypopharynx was a more frequent finding with food sensitive cases than with inhalant allergies The significance of lymphoid hyperplasia remains obscure though many theories have been propounded to explain its significance

The larynx was the site of reactions in some cases. The vocal cords would become thickened and edematous and the voice become hoarse after ingestion of noxious foods. We encountered no cases of respiratory difficulty resulting from acute edema of the cords.

DIAGNOSIS

The patient's racial, economic and religious background had some bearing on the history of food sensitivities, particularly in our practice for a large percentage of our patients came from immigrant stock. Although the eating habits of the children are considerably altered from that of their parents, certain nationality dishes are retained. For some, religious *beliefs may have an effect upon the diet.* A childhood history of colic, diarrheas, and food intolerance often point to food idiosyncrasies in later life. Likes and dislikes to certain foods must be evaluated with caution for, as a rule, they bear little relation to the patient's tolerance or intolerance of foods incriminated by the patient. Eating habits of the patient should be inquired about, for valuable leads may be obtained from such information. As a rule, there is little seasonal variation to foods, except perhaps in fall when an abundant harvest may result in reduced prices which may influence the thrifty housewife to prepare and serve such foods more often than usual.

A significant lead to the presence of food allergy in the patient under adequate inhalant therapy is failure to respond to treatment. All inhalant cases which do not respond to adequate therapy shoud be suspected of having a hidden food allergy.

Bryan and Bryan (4) have applied the in vitro cytotoxic reactions of leukocytes as an aid in the clinical diagnosis of food allergy We have not utilized this method in our practice but intend to do so. As the authors stress, the success or failure of the method is dependent upon meticulous technic in carrying out the test.

TREATMENT

We routinely employ skin tests by the scratch method for all cases with food allergy. We realize that such tests are of limited value, but when properly correlated with a good history they provide valuable information which repays for time and effort expended in performing the tests. We use the results of the tests as a guide as to what foods to eliminate

and utilize the tests as a starting point in the therapy.

Hale (5) conceived the idea of testing with material extracted from the seeds of the fruits and vegetables for which the patient was being tested. He based the rationale for the tests on the following facts.

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Skin tests are then supplemented with individual food ingestion tests as advocated by Rinkel The findings of such tests are then utilized to establish a basic diet to which foods are gradually added At times Derlacki's (6) basic diet is utilized if the patient does not do well on the original diet prescribed for him It is not enough to instruct a patient to stay away from certain foods. He must also be informed as to the sources of the harmful foods, how to avoid them and what substitute foods he can use Attention must also be taken to assure a well balanced diet with proper vitamins and minerals added

The food allergic patients whom we see in our practice are difficult to handle Since their symptoms are not as a rule severe, many do not take the trouble to embark on a rigorous regime of food elimination and substitution such as is frequently required. Then too, the patient of today expects to be cured by "miracle drugs" and resents having to do something for himself rather than to have his physician prescribe a regime of medication which will assure a cure merely by taking pills Many want to know why they can't go on eating the foods they like while receiving injections against foods as they do for dust or pollen Likewise the modern day housewife has forgotten how to cook and bake After one or two attempts at preparing a wheatless loaf of bread she gives up in despair and seeks a ready-made product at some health store where the food may be stale and unpalatable by the time it is purchased. The clinician must see the patient's side of the story and assist and encourage him as much as possible.

SUMMARY

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REFERENCES

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POLLINOSIS AND ATMOSPHERIC MOLDS
(Courses No. 3 and 4)

MICHAEL H. BARONE, M. D.
Buffalo, New York

BERNARD M. BARRETT, M. D.
Pensacola, Florida



QUESTION What molds do you feel one should skin test with?

DR. BARRETT In clinical practice, the following molds are representative and practical and are the most common offenders: Alternaria, Hormodendrum, Helminthsporium, Pullularia, Aspergillus, Penicillium, Fusarium, Rhizopus and Mucor.

Additional mold species, such as grain rusts and smuts, may be important allergenic factors in certain areas.

QUESTION What molds would you employ in treatment?

DR. BARRETT It would be physically impossible to test with all mold fungi or to combine all reacting species into treatment mixtures, even if the antigens were available. One can only hope that considerable cross sensitization exists. Universal cross immunity cannot be anticipated among all the molds, and so expediency would dictate that treatment mixtures be made as polyvalent as possible.

Thus in instances of positive reactions to several genera of the Dematiaceae, we would include them all in a therapeutic dematiaceous mixture. Similarly, in definite reactions to moniliaceous molds, we would prepare all species of these molds in a moniliaceous mixture Our experience has been that treatment mixtures containing all the reacting molds have often afforded better clinical results than have single species antigens.

Although pathogenic fungi, especially monilia, may involve the respiratory tract, they are most commonly encountered in dermatologic conditions. The types which come under consideration are, Trichophyton, Monilia and Epidermophyton These commonly cause lesions of the hands and feet and around the eyes and ears.

We employ a mixture of trichophytin, oidiomycin (monilia) and epidermophytin. The stock solution, 1:1000 (#3) is diluted serially through Nos. 4, 5, 6, 7, 8, 9, and 10. We have found that the

dilution most commonly effective is #7. (1-10 Million) For a nonspecific blocking effect on the allergic process or for staphylococcus immunization, staphylococcus toxoid may be added to the injection of fungus extract The results obtained in the use of small optimum doses has been most dramatic

A great many cases of dermatitis are encountered in which it is a question of atopic dermatitis, contact dermatitis, or a fungus (allergy or infection) and prompt initial improvement may be obtained by the use of staphylococcus toxoid, fungus extract, or a combination of both

QUESTION: If a patient does not obtain complete relief from preseasonal pollen desentization, what can be done to help him get through the season with less discomfort?

DR BARONE If preseasonal therapy does not give adequate relief, treatment is then continued coseasonally, using Hansel's optimum type of therapy. In order to institute this form of treatment, it is best to determine the degree of reactivity of the skin, by using serial dilutions in skin titration. Start with a dilution of one to ten million in adults (1-10,000,000) and one to one hundred million in children ,1-100,000,000): use only two dilutions at the time of the first visit. If no reaction occurs, the next two dilutions may be given, i e., 1-1,000,000 and 1-100,000 in 2-3 days and so on until the end point is found.

Treatment is started with a dose of ten to fifteen times the end point, and given every one to three days. If the patient responds well to a given dosage, do not attempt to lengthen the period of relief by increasing the dosage. In most cases, the coseasonal form of therapy is my method of treatment.

OPTIMAL DOSAGE THERAPY
TECHNIC OF CYTOLOGICAL EXAMINATION
(Courses No. 5 and 6)

FRENCH K. HANSEL, M. D.
St. Louis, Missouri

LINDEN J. WALLNER, M. D.
Chicago, Illinois



QUESTION Do you find nasal cytology of much practical value in private practice?

DR. WALLNER I certainly do It *gives us a good objective method for* making a diagnosis of allergy. We may suspect it from the symptoms or the appearance of the nose, but with an objective test we can be more sure Then we feel more justified in further work-up with skin tests, etc.

QUESTION· Does your technician do this examination for you?

DR. WALLNER: I spread the material on the slide and she stains it and it is ready in a few minutes, while the patient is still in the office. But I examine the slide myself, as I find this of more benefit than a report.

DR. HANSEL: (In answer to a question apparently regarding dosage of staphylococcus toxoid). . . . the dosage is based entirely upon clinical experience. In a large number of cases over a long period of time we found in using toxoid that from 1/10 of a unit up to one unit gives a stress or ACTH effect.

With a weaker dose, say to 1/100 or *to 1/1000 of a unit, an immunologic* phase is reached with immunity to staphylococcus Immunity to staphylococcus is not produced with a stress dose of staph That was our first discovery. In infantile eczema some years ago, I discovered that with this stress dose, remarkable results were obtained, then we found that the immune doses were far down the scale We have reduced doses to as low as one millionth of a unit in some cases of rheumatoid arthritis. We don't ordinarily treat patients of this type but we have experimented with it with excellent results.

QUESTION: How long will the effect last?

DR. HANSEL. The average dose will last about four days in the beginning. *Later the effect* will last from

four or five days to one week. The treatment can be discontinued if there are no symptoms after two weeks If you are using a certain dose and getting good results you should automatically reduce the dose because there may be a loss of tolerance after a few doses, a half dozen or so, and a flare-up may occur The dosage can always be increased if it is too low but if a flareup of symptoms occurs, you may have difficulty in establishing an optimal dose. A rest period of several weeks should be allowed before giving further injections.

QUESTION: In finding the optimal dosage do you use *skin titration*?

DR HANSEL: This is a very good method in finding the end point in pollen treatment but not so good with dust, except Endo dust which titrates out very well Titration is not very adaptable to the establishment of toxoid dosage

QUESTION When do you use the stress dosage?

DR HANSEL For urticaria, dermatitis around the ears or eyes, atopic or contact dermatitis, for anything in which you want an ACTH effect There are many nonspecific remedies which do the same thing, such as pyromen or anergex We have preferred toxoid because the material is well standardized and we know the range of dosage For a stress effect dosage we use less than one unit. We use 1/10 to 1/2 of a unit intradermally, rarely more than 1/2

QUESTION Just where do you find cytology most helpful?

DR. WALLNER: I find that I use it almost routinely in children So often, especially in children, the diagnosis is between obstruction due to adenoid, infection, or allergy. This is especially true where we are attempting to find the cause of a serous otitis media All three conditions may be present in the same patient The percentage of eosinophiles often determines whether we order an antihistamine or antibiotic, or both.

QUESTION: Do you titrate with histamine?

DR. HANSEL: Some work has been done on that. The average end point on histamine is #5 or #6, that is, 1 to 100,000 or to 1,000,000 We haven't done too much with it but we recommend titration to histamine in headache cases for an optimal dose and to determine whether a patient who titrates up to 1 to 1,000,000 takes a different dose than one who titrates to 1 to 100,000. The histamine reaction in the skin would depend upon that patient's skin reactivity. A patient with dermographia will react away up at #6 or #7 while a person whose skin is less sensitive will require much stronger test extracts But if you titrate a patient with histamine, one on whom you are going to do skin tests, and he gives a low point of 1 to 1,000 or 1 to 10,000, skin reactions are not likely to be good The histamine test is a good indicator of how responsive the skin is going to be to other tests In some, good positives may not be obtained, so in these patients, stronger extracts should be used The histamine titration would indicate this

OPTIMAL DOSAGE THERAPY
TECHNIC OF CYTOLOGICAL EXAMINATION
(Courses No. 5 and 6)

FRENCH K HANSEL, M. D.
St. Louis, Missouri

LINDEN J. WALLNER, M. D.
Chicago, Illinois



QUESTION. Do you find nasal cytology of much practical value in private practice?

DR. WALLNER: I certainly do It gives us a good objective method for making a diagnosis of allergy. We may suspect it from the symptoms or the appearance of the nose, but with an objective test we can be more sure. Then we feel more justified in further work-up with skin tests, etc

QUESTION: Does your technician do this examination for you?

DR. WALLNER: I spread the material on the slide and she stains it and it is ready in a few minutes, while the patient is still in the office. But I examine the slide myself, as I find this of more benefit than a report.

DR. HANSEL: (In answer to a question apparently regarding dosage of staphylococcus toxoid). . . . the dosage is based entirely upon clinical experience. In a large number of cases over a long period of time we found in using toxoid that from 1/10 of a unit up to one unit gives a stress or ACTH effect.

With a weaker dose, say to 1/100 or to 1/1000 of a unit, an immunologic phase is reached with immunity to staphylococcus. Immunity to staphylococcus is not produced with a stress dose of staph That was our first discovery. In infantile eczema some years ago, I discovered that with this stress dose, remarkable results were obtained, then we found that the immune doses were far down the scale We have reduced doses to as low as one millionth of a unit in some cases of rheumatoid arthritis We don't ordinarily treat patients of this type but we have experimented with it with excellent results

QUESTION How long will the effect last?

DR HANSEL: The average dose will last about four days in the beginning. Later the effect will last from

four or five days to one week The treatment can be discontinued if there are no symptoms after two weeks If you are using a certain dose and getting good results you should automatically reduce the dose because there may be a loss of tolerance after a few doses, a half dozen or so, and a flare-up may occur The dosage can always be increased if it is too low but if a flareup of symptoms occurs, you may have difficulty in establishing an optimal dose A rest period of several weeks should be allowed before giving further injections

QUESTION: In finding the optimal dosage do you use skin titration?

DR HANSEL This is a very good method in finding the end point in pollen treatment but not so good with dust, except Endo dust which titrates out very well. Titration is not very adaptable to the establishment of toxoid dosage

QUESTION. When do you use the stress dosage?

DR HANSEL For urticaria, dermatitis around the ears or eyes, atopic or contact dermatitis, for anything in which you want an ACTH effect There are many nonspecific remedies which do the same thing, such as pyromen or anergex We have preferred toxoid because the material is well standardized and we know the range of dosage For a stress effect dosage we use less than one unit We use 1/10 to 1/2 of a unit intradermally, rarely more than 1/2

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QUESTION. Do you use cortisone in your allergy practice?

DR. CRISPELL. It depends entirely on who the patient is and what his problem is. You can't make anything standard. This year I have used two things in hay fever, ACTH and a cortisone used in combination with triaminic, the Smith-Dorsey product which they put out in combination with hydro-cortisone. There were no youngsters in that group but there were a few adults that I have had some trouble with in the past because of their tendency to develop asthma, and for that ten-day or two-week period during the peak time I have resorted this year to the use of triaminic with hydrocortisone. It is not the type of therapy which I like and I am against using it as a routine measure.

QUESTION: Do you take your own histories?

DR. CRISPELL: Yes, I sure do; I want to know the history; I prod the mother. As soon as I decide that I am going to do an allergy examination I have the patient fill out this sheet regarding his symptoms. It helps me and it also makes the patient think. My nurse starts the skin tests and starts to talk with the patient, going over and over the history with him. She wheedles things out of him and then instead of writing it down she will say to the patient or to the mother, "Now, when the doctor comes back to check these tests, you be sure to tell that to him.' We use a sort of running history which works very nicely. So when I read the skin tests, that gives us a chance to coordinate the history again.

HISTORY TAKING
(Course No. 7)

LAWRENCE S. CRISPELL, M. D.
Joplin, Missouri



QUESTION What do you do in regard to taking an allergy history?

DR. CRISPELL: An allergy history is actually, as far as I am concerned, a running history In working with a youngster, I will start my physical exam, and while I am doing the physical exam I discuss the history with the mother I find that if I keep prodding the parent as I am doing the physical exam that I get more out of it than if I just sit down and start to take a history After I have finished my exam, we take our patient out into what we call our allergy room and then give the mother a history sheet, which I have here and have shown you, and let her start filling in the answers to this abbreviated history sheet, as we are doing the skin tests. The skin tests in my office are done entirely by my office nurse—of course, I read them—but while my nurse is doing the skin *testing*, she also prods the mother regarding the history. If she can get anything out of the mother that she feels is important, she tells the mother to be sure and tell the doctor when he returns, and of course, I go back over the history again while I am reading the skin tests On all subsequent visits we also press on history and find that many times we can stimulate the parents into thinking about things that are very important that they are not able to tell us on the first visit because they simply do not think about them.

QUESTION Doctor, do you believe that a history form as produced by Dr Jack Anderson is helpful?

DR CRISPELL Of course, there is no question in anybody's mind that Dr. Anderson's history is ideal However, I feel that the short form that we use and the running type of verbal history that I am able to get from the parent are quite adequate in my hands, and in most cases, at least, answer the questions that I am interested in. To be quite frank with you, I do not feel that I have extra time to sit down and go over the voluminous history as suggested by Dr Anderson, i.e, reading it and cataloguing it, etc, which is certainly necessary if you are going to use such a form. Therefore, I go back to my shortened form as being most adequate for me.

her? This is not allergy I would venture to say no two men around this table would suggest the same therapy.

Now, here is an x-ray of a child seven years old with nasal symptoms all of her life As you see, the sinuses are clear in the x-ray. This patient has an allergy, and not infection She was relieved of her nasal symptoms by allergic management

QUESTION: What is your surgical approach to the antrum?

DR. STAHL: I agree with Dr. Henry Goodyear that a large percentage of antral infections can be surgically cured by the window approach It is important to create a large window anteriorly, and to pack the antrum for several days.

The Caldwell-Luc procedure is a fine operation and is reserved *for those cases* that one wants to biopsy *or explore* for dental causes that cannot be excluded preoperatively.

DR SANDERS. Here is *an x-ray of* another child seven years of age. He has been sick practically all his life. His tonsils and adenoids were removed at the age of three He missed over a month of school last year and every time he joined in outdoor activities with the other children he would take a cold.

He had a dust sensitivity, a purulent discharge in his nose which contained an occasional eosinophil and, as you see, the x-ray showed a generalized density in both maxillary sinuses.

This patient was given large doses of antibiotics over a period of three weeks. The nasal symptoms cleared up in five days but returned soon after the antibiotics were discontinued. He was also being hyposensitized to house dust. Antibiotics were administered again for a longer period—five weeks. The x-ray at the end of the five weeks still showed pathology and the symptoms returned as before. However, after antral windows were made, the child began to pick up immediately In the past school term he has missed only two days of school and has required antibiotics only on two occasions

This case shows the necessity of treating both the allergy and the infection when both are present in the same patient. Each condition requires its own especially indicated type of treatment, if the best results are to be obtained

DIFFERENTIAL DIAGNOSIS
X-RAY EXAMINATION AND INTERPRETATION

(Courses No. 8 and 9)

SAM H. SANDERS, M. D.
Memphis, Tennessee

RICHARD H. STAHL, M. D.
Cuyahoga Falls, Ohio



QUESTION What is your opinion concerning the routine use of x-rays on new patients?

DR STAHL · Generally speaking this is a good idea, particularly if you take the pictures in your office or at an adjacent center where they can be examined These pictures become more valuable if we are able to examine them ourselves, not necessarily taking the interpretation of the roentgenologist

I feel that x-rays are indicated in most cases, except those with trivial or mild recent complaints. What do you think, Dr. Sanders?

DR. SANDERS: Well, let's look at this sinus x-ray of a thirteen year old girl. In the nose forward position you can see much extra space in the lower half of the nose. This would suggest an atrophic condition. There is density in the ethmoid, less density between the septum and the middle turbinate than would be expected, small frontals with uniform density which could be pathological. The nose chin position shows a thickening in the antral mucosa and some generalized density which is evidence of chronic infection

At the age of four this child was seen with bad tonsils and adenoids and a purulent sinusitis. She was seen later for ear complications We could not persuade the parents to bring her in except during an acute exacerbation She was the member of a large family living out of town and the parents said they could not afford the visit to town even though the medical service was being given free of charge.

The child was seen off and on at five, six, and seven but not again for five years. Now she has developed an atrophic rhinitis from a pansinusitis and has a chronic bronchitis with an early bronchiectasis Early treatment would have prevented this patient from becoming a respiratory cripple. What to do with

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ARRANGEMENT OF OFFICE FOR THE PRACTICE OF ALLERGY PREPARATION OF DILUTIONS (Courses No. 10 and 11)

EDLEY H JONES, M. D.
Vicksburg, Mississippi

DWIGHT D. MOFFITT, Ph. D.
Philadelphia, Pennsylvania



QUESTION How much equipment is necessary and how much time is required to make an adequate study of a patient with nasal allergy?

DR. JONES: Since most of us have this work done by our office nurse or laboratory technician, comparatively little of our own time is required Of course, we must read and interpret the tests, make the diagnosis, outline and prescribe the treatment, and give the patient full instructions.

You should have a full set of testing antigens—pollens, dust and molds, miscellaneous, and food antigens Mr. Dwight Moffitt, who is jointly conducting this Round-Table discussion with me, is connected with the Hollister-Stier Laboratories, generally recognized as a leader in this field, and he can tell you exactly what all the equipment costs, such as testing antigens, sterile rubber-capped vials, diluting fluids and all other accessories.

Scratch tests can be made with just about anything that will break the skin; a hypodermic needle, a dull knife, the Von Pirquet chisel, or best of all, the Morrison Micro-scratcher. Intradermal tests are made with tuberculin syringes and small short needles, we use 25 gauge needles, ½ inch long.

You will need a separate sterilizer for your allergy equipment, and should use only distilled water in it Of course, an autoclave is a satisfactory alternative. You will need an adequate supply of tuberculin syringes, a couple of 5 and 10 c.c. syringes, and plenty of small needles

QUESTION. In correlating dilutions and pollen units I'm never sure whether the pollen units are of each item or whether it is a combined total unitage of the pollens in a mixture.

MR MOFFITT: The most concentrated pollen extract we supply is a 1-20 dilution which contains 50,000 pollen units per cubic centimeter. If 1 c.c. of 1-20 short ragweed, which is 50,000 pollen units, and 1 c c. of 1-20 timothy, 50,000 pollen units, are combined, each c c of the mixture will contain 25,000 pollen units of short ragweed and 25,000 pollen units of timothy, making a total of 50,000 of the mixture in each c c

This holds true with any number of pollens in a mixture but there can never be more than 50,000 pollen units per c c. in the combined mixture

QUESTION. How do you go about making up different dilutions?

DR JONES· Some allergists dilute by 10's but I think most of us dilute by 5's In prescribing an extract by 10's it is necessary to give a dose of 1 full c.c of a dilution before going to the dose of 10 c c of a dilution 10 times stronger, whereas by 5's you need to give a patient a dose of only .50 c c before going to a dose of 10 c c of a dilution 5 times stronger I prefer the smaller dose

The actual dilution is mere arithmetic, when using 5's you use 1 part of extract to 4 parts of diluent to form another extract 1/5th as strong. For example, if you were diluting a 1·10 extract your succeeding dilutions would be 1:50, 1:250, and so on.

QUESTION: Why do you always advise testing with the individual pollens instead of using a mixed extract?

MR MOFFITT· The mixing of extracts reduces the amount of each antigen, and the more pollens in the mixture, the less there is of each. If you are testing a patient with a low skin reactivity there will not be enough antigen to produce a diagnostic response to any individual pollen Thus, a false negative reaction is obtained.

Only in grasses is there a family antigen Bermuda and Johnson grass are exceptions and do not share the same antigens with each other or with timothy or June or the other common grasses.

The weeds are the most specific, with very little cross reactions except in the ragweed family

Testing individually and treating specifically will give the best results.

TREATMENT OF INHALANT ALLERGY
(Course No. 12)

WILLIAM H. EVANS, M. D
Youngstown, Ohio

JOSEPH W. HAMPSEY, M. D.
Pittsburgh, Pennsylvania

QUESTION Is treatment with inhalants other than pollen often necessary in food allergy?

DR. HAMPSEY In my experience, the majority of patients with food allergy also have some form of inhalant sensitivity as well. For this reason I usually titrate them to house dust at the first visit, so that hyposensitization can be under way while a search is being made for the offending foods, either by skin test or dietary manipulation

QUESTION What dosage of house dust is commonly used in these patients?

DR. HAMPSEY Adults are often started on the 1-100 million dilution, while generally the 1-1 billion dilution is used for children After the inhalant problem is controlled by the use of house dust extract and the reduction of inhalant contacts, it is easier to get satisfactory results from food tests and from the omission of offending foods.

QUESTION: Do you depend on hyposensitization alone to control allergic symptoms?

DR. EVANS: No. Frequently complications require the use of steroids, antihistaminics, ephedrin, adrenalin, sedatives, aminophyllin and other drugs for their control.

QUESTION How frequently do you use antihistamines?

DR EVANS. Since we are primarily interested in relieving the symptoms as rapidly as possible, we frequently prescribe antihistaminics immediately. However, as soon as possible, the use of the drug is discontinued.

QUESTION How do you use staphylococcus toxoid in your allergy practice?

DR HAMPSEY Well, I have patients in whom I suspect food sensitivity at the very first visit. I can't track it down at the first visit but before they leave I am apt to start them off with an injection of staphylococcus toxoid and occasionally they are benefited for a day or two. They will mention it without being questioned And these are food cases. They get a non-specific response, I am sure, but staphylococcus toxoid just

happens to be one of the best purified vaccines that we have and one that we can rely upon in serial dilution When we are using it in 1-10,000 or 1-100,000 dilutions we like to have a well purified vaccine that we can rely upon. I usually give 1/100 of a unit as an initial dose

QUESTION · Do they get any local reaction?

DR HAMPSEY: No, not with 1/100 of a unit. I usually rely upon what they tell me when they come back. Now, as you get into that case maybe you can pinpoint the food and remove it from the diet and then the patient won't need the toxoid But the little kick he gets from it is helpful, although it may not work continuously if the patient continues to eat the food to which he is sensitive

QUESTION · Do you use steroids routinely in the treatment of inhalant allergy?

DR EVANS · No, but we do use steroids as an adjunct to other forms of treatment in an attempt to control allergic symptoms Usually this is only for a short period of time. We never discontinue steroid treatment suddenly while the patient is taking a dose of maximum size Instead, the dose is lowered gradually over a period of days or even weeks.

QUESTION Are nasal applications of steroids useful in treating nasal allergy?

DR EVANS · Yes However, they are much more effective when used as an aid to other forms of treatment, such as hyposensitization, antihistamines, etc Powdered hydrocortisone sprayed into the nose is very effective in controlling acute symptoms

QUESTION. How many plants and weeds, etc, do you test with?

DR. HAMPSEY: I use about fifteen weeds routinely. One of the most important ones in our area is Mexican Tea, especially during the last five years. It is air borne and usually precedes ragweed, coming at the end of July and during the early part of August. I've only had two cases; I wasn't able to explain their symptoms at the end of July until I learned about the importance of this pollen and tested them out with it.

QUESTION: From the standpoint generally of weeds such as dandelion, goldenrod, etc, with a heavy pollen; a person may be sensitive to them but do they really cause any symptoms?

DR ? ?: In my part of the country, in Idaho, we don't have ragweed, but we have grass and other weeds, such as Russian thistle, sage brush, sugar beet, dandelion, etc, which cause trouble.

QUESTIONER · They do cause trouble; that's the point I was getting at. Some doctors will dismiss entirely the fact that some of these heavy pollinating weeds will not cause trouble because they are not air borne, but some of them do cause trouble.

QUESTION. Will the systemic use of a steroid remove nasal polyps without surgery?

DR. EVANS. You can shrink polyps of allergic origin by administering a steroid by mouth, intravenously, or by the intramuscular route, but you should caution the patient that if allergic symptoms recur, the polyps also will return.

ALLERGY OF THE EYE; DIAGNOSIS AND TREATMENT (Course No. 13)

ROBERT S. COLES, M. D.
New York, New York

LELAND H PREWITT, M. D.
Ottumwa, Iowa



QUESTION. Doctor, what percentage of uveitis is due to allergy?

DR. COLES Certainly there are many forms of uveitis in which I think allergy plays an important role In addition to foods and inhalants, there are certain forms of bacterial uveitis in which bacteria or their products play an important role—tuberculosis, for example. We now believe that toxoplasmosis has a strong allergic component leading to a severe posterior uveitis, and allergy undoubtedly plays a predominant part in the causation of sympathetic ophthalmia I am afraid, however, when I think of allergy as causing uveitis, I don't think of it in terms of everyday practice where you can determine this allergy via skin tests or patch tests or things of that nature. I think of it on a more intricate and a more complicated level of tissue hypersensitivity

QUESTION: In sympathetic ophthalmia, besides uveal pigment sensitization, do you believe there is some other factor which causes the pathology?

DR. COLES: Well, I certainly feel that uveal sensitization plays the predominant role in the causation of sympathetic ophthalmia. I believe that perhaps there is something necessary to trigger the reaction and this necessary factor could be either a conjunctival saprophyte of no pathogenic significance by itself, or a virus, or a bacteria When entering the eye, one of these may come in contact with the uveal pigment of the uveal tract, and then combine with it, forming an entirely new substance which acts as an antigen and then causes sensitization of the other eye, leading to sympathetic ophthalmia This is purely speculation, however.

QUESTION: Why doesn't antihistamine therapy take care of the majority of allergic reactions?

DR. PREWITT: Antihistamine therapy will help a great deal in the anaphylactic and the acute reactions, but hista-

mine often is not the major factor in the delayed type of reaction. The toxic proteolysis that takes place in allergic reactions produces many various chemicals, each of which may produce a specific type of reaction in a specific flare organ. As a result we have a complex series of chemical reactions taking place and, therefore, specific therapy for each is required.

Immunologic interaction of antigen and antibodies, and biochemical alterations, take place in the cells of connective tissues, smooth muscle and nerve tissue. These changes result in the liberation into the tissues not only of histamine but of other potent biologic substances, primarily serotonin, acetylcholine, heparin and potassium. This multiplicity of factors explains why simple antihistamine treatment cannot entirely control the allergic reaction. Consideration must be given to the use of anticholinergic drugs and the discovery of antiserotonin substances. Physical contacts, such as heat, light, cold and psychogenic factors also play an important part in the therapy of allergic reactions.

QUESTION: Dr. Coles, would you mind telling us how you would treat a patient who came in with anterior uveitis, first attack?

DR. COLES: I believe this patient should have his pupils dilated because, despite the administration of steroids, posterior synechiae tend to form. I usually use scopolamine, 0.02%, or homatropine, 5%, to dilate the pupil. I administer 2½% solution of hydrocortisone or cortisone. I feel that the suspensions are better than the solutions in the treatment of anterior uveitis, and I have the patient take this every hour or two. In the evening I have him put in a steroid type of ointment.

Recently, we have begun to employ Depo-Medrol in the treatment of anterior uveitis. This is a repository form of methyl prednisolone which takes two to three weeks to be completely absorbed. ½ c.c. of this contains 20 mgs and by giving one injection high in the superior temporal quadrant of the eye, we find that it is not necessary for the patient to take steroid drops. We achieve a large concentration in the anterior ocular structures rapidly, which is effective in curbing the uveitis almost immediately. We find within 24 hours that any plastic changes that may have occurred in the anterior chamber have subsided and that the flareup itself is under control, and symptomatically the patient is infinitely more comfortable.

I might add that we have found that Depo-Medrol is extremely effective in the treatment of any form of anterior ocular inflammation. We use it with remarkably good results in scleritis, in keratitis and in patients who have developed graft sickness following corneal transplantation.

FOOD ALLERGY
(Course No. 14)

WILLIAM H. BARRY, M. D.
Kansas City, Missouri

SYLVESTER C. MISSAL, M. D.
Cleveland, Ohio



QUESTION What effects do antihistamines have upon food allergy?

DR. MISSAL In my experience, antihistamines do not exert much effect upon alleviating the symptoms due to food allergy.

QUESTION How soon after the ingestion of food can symptoms occur?

DR. MISSAL: The time interval varies from an hour or two to 24 hours before symptoms occur In the case of the ingestion test, you get more of an explosive immediate reaction whereas in the case of food taken over a prolonged period of time, you get a delayed cumulative reaction.

QUESTION: What is the shortest period of time required to develop tolerance to an omitted food?

DR. BARRY: It has been proven by Rinkel and others that tolerance to an omitted food may occur in as short a time as 12 days.

QUESTION: What do you mean by escalator type of addition to the diet?

DR. MISSAL. The escalator type is the gradual step by step addition of foods

QUESTION: Do you place much reliance on skin tests in food allergy?

DR. MISSAL: Yes. In the first place I feel a large number of positive tests on the skin is not hyper-reaction in the sense of giving false positives. I find that such an individual is likely to be allergic to foods

Of course, the most important thing when utilizing skin tests is to correlate the patient's history with the tests There is a concomitant interaction between foods and inhalants Certain inhalants, such as pollens, enhance and aggravate the reaction of the individual to food and he may give a history that he is allergic to certain foods only during the pollen season

QUESTION: Should you use scratch or intracutaneous testing for foods?

DR BARRY: In the first place, as far as foods are concerned, neither is too

accurate. However, I do believe they are of some help and I prefer the scratch tests for the following reasons: (1) They are much safer; a severe reaction is a rarity. (2) The average accuracy of scratch tests is higher and they are less likely to give a high percent of false positives.

QUESTION: Is condensed milk less likely to produce symptoms than raw milk?

DR. MISSAL. Certain patients find it possible to use condensed milk but cannot take raw milk. In the majority of instances, however, condensed milk has about the same allergenic properties as does raw milk. We advise our patients to stay away from cow's milk entirely. The same applies to powdered milk There are some patients who can utilize powdered milk but who are sensitive to whole milk.

QUESTION Does food sensitivity often cause otitis externa?

DR MISSAL I would not say that it often causes otitis externa but certainly I have patients in whom food sensitivity does manifest itself by a skin rash in and around the external ears This undoubtedly is a form of eczema which is related to foods.

QUESTION What food do you feel is the hardest for the patient to eliminate completely from his diet?

DR BARRY Corn is unquestionably the most difficult because corn syrup and corn starch are in innumerable products, such as ice cream, medicines, most canned fruits, and juices. In fact, the list of corn-containing products is almost fantastic.

QUESTION: What are some of the commonest symptoms to food allergy that you have noted in your practice?

DR. MISSAL. I feel that the throat manifestations are the most common and the most significant. It is natural that this should be the case because ingested food comes in contact with the mucous membrane of both the oropharynx and the hypopharynx on its way down to the esophagus. I have found that dull aching sore throats have frequently been associated with ingestion of noxious foods Also the appearance of the throat is rather characteristic. There are islands of lymphoid hyperplasia. The mucus membrane is dull red in character and frequently resembles the smoker's throat which you are all acquainted with I have frequently been amazed to get the history out of such patients that they do not smoke at all; yet their throats are typical of that of a smoker. I feel it is an irritative phenomenon where the shock organ, or the shock tissue rather than a specific organ, is the mucous membrane of the throat. Food can, of course produce generalized allergic reactions just as inhalants do, but such reactions as asthma or severe rhinitis are far less common with foods than they are with inhalants

REPOSITORY THERAPY IN ALLERGY

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I have been forewarned by your program committee and by your Council that you are a very attentive and critical group. The evidence of your attentiveness has been demonstrated this morning and before you become too critical of me I will admit that I do not know all the answers in the use of emulsified extracts. I enjoyed your program this morning. I am sure you have enjoyed and benefited from the Round Tables I have no slides and I have no aids other than some pictures which I will pass to you.

In the past it has been recognized that during every hay fever season something new comes up as the answer to the treatment of the allergic patient By "answer" I mean the answer to the problem of the allergic patient so that the specialty of allergy apparently would be doomed. I think that was true with the introduction of antihistamines. The same thing happened with the steroids. Now with the use of emulsions in the treatment of inhalant allergy, there is again a scare program that this might be the answer to the complete treatment of the allergic patient. This is not the total answer to the treatment of the allergic patient; it is simply an easier and a better way to take care of the allergic patient.

As an introduction, may I take the liberty of reading definitions of terms and phrases which will be using during the time that emulsions are discussed. In the first place, an emulsion may be defined as a suspension of an oleagenous or resinous material in an aqueous liquid; or as an aqueous liquid in an oil with gum or a similar agent; or as a dispersion of fine particles or globules of a liquid in a liquid. There are two phases to an emulsion. One is the dispersed phase; that phase of a substance in which the material, in finely divided particles, is in a state of suspension in some other substance is called the continuous phase or the dispersion media. The continuous phase is that phase of a substance in which other phases are dispersed. Syneresis is the contraction in a gel on standing, with or without exudation of the liquid; it is a drawing together, a contraction of a clot. The exudation of the liquid constituent of a gel is irrespective of the vapor pressure imposed on the system, and lowered vapor pressure aids the process of syneresis. Now, if I have you as mixed up as much as I am after reading this, you will see why I am going to talk to you on *how* these emulsions should be used clinically, leaving the *reasoning* for their use to those who know more about emulsion chemistry.

The treatment of inhallant sensitivity for pollens, molds, dust and other materials has been very satisfactory with conventional multivisit therapy In the past, the investigators have always been trying to find easier, better and safer ways for the administration of these extracts This work with emulsions has been done over a period of the last fifteen or twenty years It is not new; this is not a new treatment, but a new application of established principles The processes have been perfected to the point where they are safe, but they are not available for general use. In the past, the employment of extracts in the treatment of inhalant allergy has always been pointed toward the prolongation of the effect or the use of the extract in a way that will permit less visits and make it easier for the doctor as well as for the patient Mary Loveless was the first one to apply and extend the treatment of pollinosis after the original work of Freund and McDermott with mineral oil Subsequent to Mary Loveless, Ethan Alan Brown and others have been using emulsions in the treatment of pollen sensitivity and inhalant sensitivity

It is important to realize that oil and water will not mix but for emulsion preparation an emulsifying agent is necessary Various oils and various emulsifying agents have been employed The ones that I have been using under the direction of those who know much more about this than I, are Arlacel A, the emulsifying agent, and Drakeol which is the mineral oil This is supplied as one part Arlacel A and nine parts of Drakeol I have the material here and later I will try to demonstrate the preparation for you so that you can see the material and be familiar with it It is very important in treating any patient with seasonal hay fever to realize the variables which must be considered in the treatment of that patient. First of all, how sensitive is this patient? He reacts to the material with which he is tested or he reacts to the material in his environment in a clinical way because he is sensitive to it.

The method of administration of injectable extracts is a matter of concern to the physician It is recognized that the order of safety in which any injectable material (and particularly, allergenic extracts) are given is intraspinously, intramuscularly, subcutaneously, intramucosaly and intravenously These emulsified extracts are given subcutaneously. They can be given intramuscularly but by this route the material produces a greater degree of local reaction and response When given subcutaneously, the local reaction, if any, is very minor The concentration of pollen extract used in the conventional multivisit type of treatment is one variable which influences the presence of constitutional reactions. The degree of activity of the material that is being used is another. In other words, it is more satisfactory to treat a patient with grass pollen sensitivity than it is to treat a patient with ragweed pollen sensitivity The grass pollen extract has less "fire" in it than does the ragweed extract The ragweed pollen itself is much more active in the production of symptoms than is the grass pollen The patient with ragweed pollen hay fever is much more uncomfortable than is the average grass pollen sensitive patient with symptoms during the grass season. And then too, we must consider the amount of material that is given in treatment of these patients and the frequency of administration of the extract All these variables are considered in the use of

emulsions in the treatment of these inhalant conditions.

There are other variables that must be considered from a clinical standpoint. It has been stated that children tolerate increases in dosage better than do adults, the amount of reaction is less, both constitutionally and locally The material injected is important; ragweed is more likely to produce a constitutional reaction than are other pollens, dusts or mold extracts. The time of treatment as far as the season is concerned is important This so-called repository emulsion treatment has also been termed opsiphylactic, which is a big word meaning "time" or "at the proper time." These emulsified extracts must be given at the best time—prior to the expected onset of the season, as I will tell you later The most important thing, however, if you are using multivisit therapy, is the response to the last previous dose. You judge your dose today primarily upon the patient's response to the dosage he had a week ago, or four or five days ago, or two weeks ago, whichever is your schedule. Slow absorption is important. The work that has been done by various investigators using lanolin, mineral oil, almond oil and various forms of extraction and fractionation of pollen extracts, has been pointed toward slow absorption. Because it is slow, it is prolonged absorption

I know of no definite method that will tell me or give me any real basic information concerning how sensitive a patient is to the material that is being used. Because of the absence of any well based method by which the accurate *degree* of sensitivity can be established or determined, I know of no way to accurately judge how much extract to give a patient. We can skin test these patients, we can determine their *apparent* degree of sensitivity by their history but in summation, it is your own clinical judgment that determines the dosage for these patients. The dosage schedule is based on how the individual patient responds to treatment. In other words, you must individualize the treatment of your pollen sensitive patient whether you are using conventional multivisit therapy or whether you are using emulsified extracts There are some variations in materials that are required. An emulsion requires the use of nonglycerinated extracts. There is no true correlation, although this is debatable between the patient's clinical sensitivity, his ophthalmic response to testing, his skin test reaction size, the size of the dose and finally, the degree of protection or immunity that is produced. So again, how do you judge the dosage for a given patient? How much do you think that patient can stand within the limitations of safety and protection for him?

For demonstration of an emulsion, the easiest way would be for me to show the material, let you see the manner in which it is prepared, realizing of course that there are variations to this. Experience has shown that emulsified extracts are safe, sound, and satisfactory. The physicians having severe reactions or difficulty with emulsified extracts are those who have made variations upon their own without realizing what they were doing or without knowing the reasons for the modifications. I think it is imperative to have a definite planned procedure in the preparation of the emulsion.

In the past month or so there have been publications stating that an emulsion can be made in two minutes or three minutes, or that you can "tell" when an emulsion is good. If you do intend to use emulsions, you should set up a definite schedule of preparation and not vary

from it, but first become familiar with the technic. These emulsions are safe; if it is a so-called "perfect" emulsion there is small chance of harm that can be done as far as reaction is concerned. The reaction, or the percentage of reactions, is less with the use of good emulsions than it is with the use of the conventional multivisit, aqueous, glycerinated type of extract.

Arlacel-Drakeol is supplied in a sterile vial so it is not necessary to Seitz filter it for sterilization You can, if you prefer, but it is prepared and available to acceptable investigators in a vial, such as this, conctaining 2 c c. of oil To prepare the material for emulsion, the pollen extract can be added to the oil in this vial. For example, if we wish to have a final strength of 2500 PNU/ml, such a strength of emulsified extract could be obtained as follows: to the 2 ml of Arlacel-Drakeol there is added 1 ml of 10,000 PNU pollen extract and 1 ml of buffered saline as a diluent—or originally 2 ml of ragweed extract 5000 PNU/ml strength Thus in the 4 ml of material there are 10,000 PNU of pollen extract giving a final emulsified strength of 2500 PNU/ml It is necessary that all of the glassware used in the preparation of an emulsion be cleansed with a detergent There are several things that will destroy the emulsion. In other words, glycerinated extracts cannot be used because glycerine will destroy the emulsion Alcohol will do the same thing; detergent will do the same thing, rubber will do the same thing The stopper on this vial is not rubber, therefore, but is neoprene It is easier to use a throw-away needle than to have a technician clean a non-disposable needle

There are several ways of making an emulsion and I want to show you a method which has proven to be simple and sound. An emulsion can be made simply by shaking oil and water, a temporary emulsion that will settle out immediately, with the oil phase and the liquid phase being separated. This vial now contains a temporary emulsion made just by shaking it. But the reason that it is not satisfactory to use as it is, is because it is not stable and it will immediately break down. In other words, this is not a "good" emulsion. As soon as the oil-water mixture is placed into this larger syringe, we will put an emulsifying needle on it. The emulsifying needle is a double-headed needle of 18 gauge dimension. In other words, it is an 18 gauge needle with a head on each end. The usual technic is to run this on the machine for approximately forty-five to sixty minutes, change to a smaller needle because of the turbulence and force that will further emulsify it and finally to a twenty-two needle, if necessary to obtain a finer degree of droplet size. Ideally the droplet size is very, very small, one micron or less in diameter, so that the so-called liquid phase of this emulsion is practically non-existent The perfect emulsion is one in which every droplet of liquid, the ragweed extract so to speak, is coated with oil When this material is given subcutaneously it's set—for example, the material is given here (see drawing) and it sets in these droplets, like so, packed very, very tightly. What we want, and what eventually is going to happen is that the macrophages, etc., are going to rupture the oil overcoat and release the extract to be used by the patient. When these oil droplets have begun to rupture, from that moment the patient is being treated every fraction of every second whether he is asleep or awake, because the rate of absorption is constant.

The more small droplets you have, the better is the emulsion, the better will be the treatment and the safer it is. In other words, it is very much as if you had a silver dollar in one hand and one hundred pennies in the other. If you are going to put a coin into a slot machine and get one play from each coin you could get one hundred plays from the pennies while you could only get one play from the dollar. If you have one hundred droplets you get one hundred so-called units working but if you have only one big droplet you have only one unit The smaller the droplet size the better it is and the safer

All of the syringes, vials and needles used in the preparation of emulsions are kept separate from the other material in the office. We want everything to be used only for this, so that anything that is being used today with a glycerinated extract, for example, will not be used tomorrow with the emulsion.

This is a double headed needle, with one head locked onto this syringe. We will lock another 10 c.c syringe on the other end. Now we are ready to start our emulsion. It is done by pushing the material back and forth from syringe to syringe. This can be done with the hands until the material becomes emulsified Now it's more difficult. If we were to inspect it now, microscopically and by other test methods about which I will tell you, we would see that the droplet size is not uniform. If we work it for the amount of time we know is necessary, forty-five to sixty minutes on this gauge needle, and then change to a smaller gauge needle, inspection would show that the emulsion is more uniform and of smaller droplet size. Now, pass this around and "get the feel" as it is worked back and forth; then I will make another one and put on a smaller gauge needle and you can compare the difficulties of manual operation.

It is necessary to remember that when you are treating a patient who is sensitive, we will say, to both grass and ragweed, these two extracts can be given in a single injection, if you are using conventional multivisit treatment. But if you are using emulsified extracts, it is necessary to give them as single injections of the individual antigen. In other words, the patient who is both grass and ragweed sensitive should receive his grass treatment at the proper time and also should receive his ragweed treatment at the proper time. As far as the schedule is concerned, the optimum time is four to six weeks before the expected onset of the particular season. In other words, the treatment for tree pollen sensitivity should be in February if the tree season begins in early or middle April. The grass patients are treated in April, with the expected onset of the grass season in Iowa, where I live, being perhaps in the latter part of May. Ragweed is given in June and July, mold in January and February, and dust at any time, but preferably in the fall; in other words, about four to six weeks before the expected onset of the season. When the emulsion has been prepared and when the dosage has been determined, the emulsion is taken from this syringe and given to the patient by subcutaneous administration. As I have stated, all of the syringes are first washed in a detergent, cleaned, rinsed and autoclaved before they are used with these emulsified extracts.

Clinical results with emulsified extracts, according to Mary Loveless, are about the same as they are with conventional multivisit therapy. She states it is just an easier way to treat pollen sensitivity; other investigators say it is not only

easier but results are better. I think I will have to go along with the group that says the results are better by this method of treatment than they are by the conventional multivisit type of treatment. During the pollen season of 1959, I treated 239 patients with emulsified ragweed extract All 239 of these patients were clinically sensitive to ragweed. They were given ragweed emulsions between July 7 and August 4, admittedly late. Those who were treated after July 15 or in August were informed that they probably would have some trouble. It was hoped that their season might be shortened The dosage was admittedly low because this was "new territory" to me and I was cautious. The season was late as far as the best time for the treatment was concerned These 239 patients were all ragweed sensitive by scratch test and by history, but there was no effort made to consider other sensitivities. The patients may have been grass or mold or dust sensitive, but these extracts were not available to me for repository use at that time The dosage in these patients varied from 1500 to 2500 protein nitrogen units per c c of emulsion Other investigators have used doses ranging from 7500 to 10,000 PNU per c.c Most of this work has been done on the east coast and I think it is an entirely different problem there than in our middle west where the pollen concentration is so much heavier In these 239 patients, there were six reactions I am sure you have all been concerned with the safety of this method of treatment and with the number of reactions that might be expected

Let me tell you about these six reactions One young man was seen at nine o'clock in the morning, was tested and was given his injection of emulsified extract, after which he went home It was a hot, muggy Saturday morning and when he arrived home he had two cans of cold beer. He went out to the country club, had a scotch and seltzer, and went out to watch a golf match. He followed the match for three holes, then came back and decided to play golf himself. He had another scotch and seltzer and on the second hole of his own golf game he had an attack of generalized urticaria. In retrospect, I think the reason for his reaction was not the dose of ragweed extract—and I can't tell you now what it was except that it was between 1500 and 2500 units—but I believe the cause of the reaction was the ingestion of alcohol These patients should not use alcoholic beverages on the day upon which they receive the emulsion However, enough inflammatory reaction is set up by the second or third day to permit the ingestion of alcohol, and to protect the emulsion from destruction.

Two other patients had urticarial reactions approximately three to four hours after the administration of the emulsions For these two reactions, I have no explanation. They were treated from the same supply of emulsion as had been those patients who showed no reactions and who were in the same so-called dosage classification These first three reactions were urticarial in type They were characterized by generalized urticaria, itching and facial swelling, but these patients had no respiratory symptoms as part of the reaction picture

Three reactions were my fault. These patients had their reactions approximately thirty to sixty minutes after the administration of the emulsion The patients were seen on a Saturday morning, they were patients who never before had been seen in my office and who never had been treated for pollen sensitivity. They

were tested by the scratch method, and were checked by intradermal tests to gain an estimation by titration, if possible, of their degree of sensitization. They were also tested for the ophthalmic response. The patients, therefore, were tested by scratch, intradermally and by eye drops; the emulsion was given, and within twenty to thirty minutes constitutional reactions were noted. I believe these were due to the amount of work that was done rather than to the emulsion itself. I say this because the reactions were not characterized by urticaria These three patients had reactions that were respiratory in type. They had bronchial asthma and marked symptoms of hay fever, even though their histories showed no symptoms prior to ragweed exposure and this was about the middle of July.

The results in 1959 are based upon patient expression of relief at the time of the season or immediately after the season This, admittedly, is not a realiable method of measurement. Some investigators say that the response to treatment is a failure if the patient uses one tablet of antihistamine, or one tablet of a bronchodilator drug. Other investigators will accept the patient's expression of his degree of relief if that expression is given during or immediately after the season. The patient's judgement regarding the severity of his seasonal hay fever and seasonal asthma is influenced a great deal by the time at which he is questioned In other words, the patient who is asked today, in October, how bad the 1960 season was, may say, "It wasn't bad"; about like pregnancy or labor pains. On the next day, or a week or so later, he forgets how uncomfortable he was during the season. But if you ask a patient during the season, or immediately after the season, a more honest and accurate expression of the degree of relief will be obtained.

Now, as to the results in these 239 patients in 1959, fourteen of them must be reported as total failures; they had no relief whatever from the use of the extract in emulsified form. Let me explain one of the failures. One patient was given her emulsified extract on a Monday and on Friday or Saturday she reappeared in the office with a hot, swollen arm. She returned a few days later after using ice applications. She still had a hot, swollen arm with fluctuation in the center of the area. She had an abscess. This could not be explained on the basis of the technic that had been used. Other patients using that same source of emulsion had not reported abscesses. The technic had been sterile and I was greatly relieved when the mother of this patient asked if I thought that the series of furuncles that she had been having had anything to do with this. I believe that some of the surface staph were carried into the injection area In draining the abscess, the surgeon reported that the emulsified material drained out with the purulent matter. She was not protected, but I included her as a failure because she was given the emulsion. 32, or 13%, of these patients had results classified as fair 117, or 49%, had excellent results In my estimation, a patient has an excellent result if he takes less than 12 or 18 antihistamine tablets during the season to assist in relieving his symptoms of hay fever. 76 of these patients reported perfect results; their seasons were completely erased, and they had no symptoms of any type

Dr. Missal stated this morning that the patient who has marked nasal congestion, regardless of cause, is a toxic looking patient But, surprisingly, none of these

patients, even the failures, looked toxic even at the height of the season. They *looked* well, though their symptoms may have been present in the degree I have reported to you. 196 stated that they were better with the use of the so-called single injection of emulsified extract than they had been on whatever method of treatment they had used in 1958 At this time I am unable to tell you how many of those 239 patients had been treated by conventional multivisit therapy in 1958 28 of these patients were the same as they had been before treatment but they were completely satisfied because they had received their treatment in a single injection and in a single visit to the office rather than coming in at intervals of every 3 or 4 or 7 days 15 of these patients were worse than they had been in 1958 on whatever form of treatment they had received In 1960, 233 of these 239 patients returned for emulsion treatment Of the 6 who did not appear, 3 were probably disgusted with the method of treatment and 3 had moved out of town

It can be stated that the patients who were treated in 1960 for tree pollen sensitivity with tree pollen emulsified extract, received 100% relief of symptoms The tree pollen season in my part of Iowa is short There are few tree sensitive patients in comparison to the grass and ragweed population; there are few patients who have tree symptoms of sufficient degree to warrant treatment Those who were treated, received 100% complete and total relief of their hay fever symptoms from tree pollen sensitivity. Here again, the tree emulsion must be individualized In other words, the correct emulsion must be given as indicated for the patient's sensitivity. If the patient is oak-elm sensitive, the two can be mixed, but if he has only oak pollen sensitivity a mixture of tree pollen emulsions should not be given.

The grass pollen sensitive patients were easy to treat with emulsified extracts in comparison to the multivisit type of treatment. They were 100% relieved I cannot recall a patient who admitted having symptoms during the grass pollen season These patients were both clinically and skin test sensitive. The ragweed treatment results of 1960 are not available now but they should compare favorably to those received in 1959, and perhaps better, because of the more optimum time at which the extract was given this year as compared to last year.

In using emulsified mold extracts it is necessary that the extract be aqueous rather than glycerinated These extracts in any form seem to be irritating. The dose must be lower than might be expected The results have not been 100%, as in grass and tree sensitization, but the percentage of good results is extremely high In all of these patients it must be remembered, as Doctors Missal and Craft pointed out this morning, that the patient must be treated totally Relief cannot be expected by treating the patient only for mold and ragweed sensitivity, if he has a complicating food allergy, or if he is sensitive to other environmental materials

Dust treatment by emulsified extract is definitely worthwhile. Some dust extracts seem to be more irritating than others when used as emulsions but the results are exceptionally good. The patients and the doctor are well satisfied because of the ease of treatment.

The use of emulsified influenza vaccine in the patient with intrinsic asthma or in the patient with symptoms from a viral source, is produtcive of excellent

were tested by the scratch method, and were checked by intradermal tests to gain an estimation by titration, if possible, of their degree of sensitization. They were also tested for the ophthalmic response. The patients, therefore, were tested by scratch, intradermally and by eye drops; the emulsion was given, and within twenty to thirty minutes constitutional reactions were noted. I believe these were due to the amount of work that was done rather than to the emulsion itself. I say this because the reactions were not characterized by urticaria These three patients had reactions that were respiratory in type They had bronchial asthma and marked symptoms of hay fever, even though their histories showed no symptoms prior to ragweed exposure and this was about the middle of July

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sions can be prepared so that the droplet size is less than ½ micron in diameter - a very small droplet, indeed.

DISCUSSION

QUESTION: What dose do you use each year in pollen cases?

DR HALPIN This is an individual problem, there is no set dosage as far as the amount that can be used or is used on any particular patient When you see a patient to whom you are going to give extract in any form, you individualize that problem and give him what you think he needs or employ any method to determine what his dosage might be. The same thing is true with emulsions In using emulsified extract you are giving what is representative, we'll say, of the total dosage that will hold him for the season, and the beneficial effect, if any, is a result of prolonged slow absorption over a period of time

QUESTION: What dosage do you use?

DR HALPIN. The dose in 1959 varied from 1500 protein nitrogen units to 2500 nitrogen protein units I had read somewhere that if the patient reacted to ragweed by scratch method of testing, then that patient should not be given more than 1500 protein nitrogen units of emulsion. That is incorrect but I believed it, and I was not corrected in my belief until after I had treated the twenty-five or thirty patients last year who received 1500 or thereabout protein nitrogen units of emulsified ragweed per cc The more you do of this the braver you get so I increased the next few to 2000, and then to 2500 This year my dosages have gone higher because I have felt that if the patient did well at 2500 units I would give him 2500 units, if he did not do so well at 2000 I would raise the dosage and compare the results at the end of this year. Now that comparison has not been made because this season has not been over a sufficient length of time to permit the work.

QUESTION: Would you increase the dose on each patient the second year or the third year?

DR. HALPIN: I think this depends upon what happens, what result is obtained, whether it would be decreased or increased or whether it would remain the same Those investigators who have been using emulsions—and I say this as a belief and not as a confirmed statement—have been using dosages as high as 7500 or 10,000 protein nitrogen units per cc of emulsion. These men are lowering the dosages in an effort to see whether or not the dosage level is really the factor that matters In other words, if the patient did well on 7500 units, this year the patient will get 6000 or 5000 and if he doesn't do as well on the decrease, the dosage will go back to 7500.

As far as the dosage for dust is concerned, I don't believe there is any method of determining how dust sensitive a patient may be. What irritating properties are in the dust extract that might give a false or a misleading local reaction on skin testing? I know of no way to determine whether the patient's complaints today are due to his dust sensitivity or to whether, as Dr. Missal and Dr Craft mentioned this morning, they are due to other things in the patient's environment and diet. Here is a patient who shows a positive reaction to dust on skin testing; on allergy study he shows a positive reaction to dust; on scratch test he shows a positive reaction to dust on high dilution So you assume that the patient is sensitive to dust, but I know of no way to accurately determine this

results. The dosage is low. The maximum dosage should be 125 C C A units in ½ c.c. of emulsion. This, you will realize, is about ¼ of the initial dosage or the single dosage that you may give with the usual type of influenza vaccine. The enhancing effect of the emulsion, because it does enhance the effect, makes it mandatory to use only ½ c.c., or less, of the vaccine. In other words, if we are going to add 2 c.c. of influenza vaccine to 2 c c. of oil, and are going to give ½ c c. of this emulsion, this is actually ¼ of the suggested dose that we are giving.

It has been stated that the full effect of the emulsified extract is not reached for approximately 2, 3 or 4 weeks after the emulsion has been given. The time interval is dependent upon the amount of emulsion that is given. The extract should be given in doses of 1 c c In other words, if a dosage of 3000 protein nitrogen units is to be given, it is better to give 1 full c.c. containing 3000 units than to give ½ c.c. of a preparation containing 6000 units per c c

With the use of emulsions in the past, the patients were kept in the office for a period of 2 or 3 hours after their emulsions had been given This was a source of inconvenience both to the patient and to me. *This year, because it is recognized* that if a reaction is to occur, it will not come for 3 to 4 hours after the administration of the material, the patients have been excused as soon as they have received their emulsions. They are *instructed to report* any change or any sign of reaction regardless of how insignificant it may be.

It is advisable to remember that we may have to revise our line of thinking as far as the treatment of the pollen sensitive patient is concerned. The thinking has been that the patient who is extremely sensitive to pollen extract can not receive as much dosage as the patient who, clinically and by tests, seems to be somewhat less sensitive. A revision of our line of thought regarding pollen treatment would suggest that maybe the patient who is most sensitive requires and can receive a higher dose. With the use of emulsified extract, and with the preparation of good emulsion, that dosage can be raised safely and conveniently Emulsified extracts may not be the final answer to the treatment of pollen sensitivity, but I do think it is the better and easier way to treat the pollen sensitive patient.

Regarding the economy of this, there has been some concern expressed in a communication that most of us receive as to what is going to happen to the allergist as far as his economy is concerned. That is minor, I assure you.

This is a good way to treat the pollen sensitive patient. It's an easy way to treat the pollen sensitive patient, but I would suggest that you become entirely familiar and acquainted with the preparation of emulsions, with the manner in which these emulsions are tested, with the use of emulsified extracts, and when they are indicated and when they are *not, and then wait until the bugs and* stumbling blocks have been removed. Then you will accept it and you will like it.

I have some pictures here of good emulsions and of bad emulsions. A good emulsion is one that is prepared with the droplets being of uniform, minute size. If there is variation in them, the emulsion should be further emulsified until the droplets are of uniform size and small, or the emulsion should be discarded. The red blood cell, I believe, is 7 microns in diameter. Present day emul-

any non-seasonal trouble. My hay fever ends with frost; the end of the season is the end of my hay fever and I don't have any trouble until the following year" He is the patient, in my mind, who isn't quite as sensitive as the other example So therefore, I am going to be a little more careful with the highly sensitive patient, the same as you would be, than I am with the patient who is not quite so highly sensitive. First of all, I consider the history, secondly, the size of the skin test reaction, although it is admitted that the size of the skin test reaction does not tell you how sensitive the patient is, whether the test is by the scratch or intradermal method But it does give an indication of the sensitivity this patient has for that particular extract So the dosage, therefore, is determined by history, by the size of the skin test reactions, scratch or intradermal, and by what I *think* he needs, by what my clinical judgment tells me this patient can safely tolerate The strength of the emulsion itself is determined by how much is put into it. In other words, if into 2 c c of oil, I put 1 c c of ragweed of 10,000 P N U strength and 1 c.c. of diluting fluid, I'm going to end up with 4 c c of 10,000 unit strength. The total is 10,000 regardless of the volume. So each c c of emulsion is going to be 2500 P N U strength.

The same is true that if I want to make a 10,000 P N U per c c strength of emulsion, I will have to put in 40,000 total units into the total of 4 c c Remember, the volume of emulsion to be given should be 1 c c If you wished to give, for example, 2500 P N U and gave ¼ of 1 c c of 10,000 P N U strength, the volume would be considered inadequate So the strength of the emulsion is determined entirely upon the strength of extract used in preparation.

QUESTION: How often do you give dust injections?

DR. HALPIN: I give them as often as it seems necessary. When I give a dust injection, the patient is told to return in six months, or sooner. If he comes back in six months and he is all right, I tell him to let me see him when necessary. He may come back in six months, he may come back in a year, or longer.

QUESTION: When do you retest?

DR. HALPIN: I use retesting as a follow-up study. If I am busy and a patient comes in, I may titrate him or check him because this gives me some slight information and I find that he will wait more patiently However, I seldom, if ever, "Re-study" a patient, if that is your question

I believe there is a decrease in the size of the skin reaction with emulsion therapy I have never been able to see a decrease in the size of the reaction from conventional multivisit therapy.

QUESTION How often have you seen any constitutional reaction?

DR. HALPIN Well, there were 6 reactions in 239 patients in 1959 and fewer this year I think that I can make a better emulsion today than I could a year ago because I have had the year's experience I am more aware of reactions and what to do to prevent them. There have been more local reactions from mold extracts because they are irritating When the dosage was decreased to 1,000 protein nitrogen units or less, the local reactions were not marked The most severe reaction I have had, if I may take just a minute, was in a patient who was bee-wasp sensitive. There is no way I know to determine whether or not a

other than by the patient's statement that: "When I clean house I am worse or when I am exposed to dust I am worse." I know of no sure way of determining whether that patient's symptoms today are due to his dust sensitivity other than by clinical experience. And if you treat him for his dust sensitivity and he doesn't show a good result, he is included as a failure regardless of whether it is emulsion or multivisit type, when maybe his symptoms weren't of dust origin in the first place.

QUESTION: What dose for dust did you use?

DR HALPIN: I will have to do a little explaining for this reason, I have used a dust extract that has been supplied to me by a commercial laboratory for an investigational study. This dust is standardized on a basis of protein nitrogen units. I think talking about measurements and standardization of extracts is pretty much like asking, "How far is it from here to the door?" Someone will say, "It's thirty-six feet," and someone else will say, "No, it's twelve yards," and someone else will say that it is so many meters. We are all talking about the same thing but with a different method of expression. When I say I used 2500 protein nitrogen units of this commercial dust, then my next statement is going to be misunderstood Two other dust extracts which I use, from private laboratories, are both measured in milligrams of dust per cubic centimeter (weight by volume). To be specific and answer your question, my top dosage of commercial dust has been 2500 protein nitrogen units per 1 c.c. of emulsion and the dosage of the emulsion is always 1 c.c., so the patient receives 2500 units The top dosage with weight volume standard has been 0 2 mgs. per c.c. of emulsion.

QUESTION: How about ivy extract in emulsion?

DR. HALPIN: I don't know because that is an entirely different problem—an inhalant allergy compared to a contact type of sensitivity. My only expression here is that I don't believe in the treatment of poison ivy sensitivity by extract injection; perhaps for protection, but certainly not in active treatment of symptoms. Maybe I am wrong.

QUESTION: How long are the results from emulsion therapy effective?

DR. HALPIN: I can only say that the patients in my office are told that the anticipated life of the protection that they are receiving is anywhere from 8 to 12 months. I hope that the extract will carry them well through the season. If a patient had a good result in 1959 and a 100% result in 1960, I won't treat him in 1961—a trial without treatment. The patient who receives an injection of emulsified dust extract may have relief for a year or longer.

QUESTION. Please explain how dosage and strength of emulsion is determined

DR. HALPIN: I wish I could explain how the dosage is determined. As I said today, you must consider the history of the patient. I think the patient is a little more sensitive who says, "I have hay fever for about two weeks and then I have a horrible time with asthma. My symptoms continue into the winter. I miss two weeks of work and I am forced to sit up at night." In my mind he is more clinically sensitive than is the patient who comes in and says, "I am having hay fever but I get by; antihistamines give me some relief and I have never had any asthma; I have never had

next emulsion is 98% perfect; that leaves 2% free This leaves only 1% difference But to the highly *sensitive* patient, it is 100% difference. The variables are the patient and the purity of the emulsion My statement implies that if the emulsion is a good one, it is safer than the average injection of any extract in any dilution and in any amount.

QUESTION. If a patient is sensitive to six weeds, do you give an emulsion for each separate weed or how many do you put together? You stated that we should avoid mixtures

DR. HALPIN. I don't believe I have ever seen a grass sensitive patient who, when he was tested for timothy, orchard, June, redtop and other grasses, failed to show multiple grass reactions *In other* words, if they are grass sensitive, they are *grass* sensitive I would *treat him with a standard* grass mixture, i e, standard for Iowa or the middle west So I would treat him for timothy, orchard, June, redtop and what have you There is no Bermuda grass in Iowa so I wouldn't put it in even though he reacted to it But here is a patient who is sensitive to ragweed, Russian thistle, marsh elder and cocklebur. He begins to have his trouble on the ninth day of August and it ends on the twenty-fourth of September I am going to treat him for ragweed *There is no Russian thistle* in Iowa There is not enough marsh elder to bother that patient. There is no cocklebur; he shows reactions because they are in the same family. For the patient sensitive to oak, elm and maple pollens, I would treat him for all three in one emulsion If we are going to give him 3,000 units, we will give him 1,000 units of each in emulsion in the 1 cc. But it would be unwise with a patient who reacts only to oak and whose history is compatible with the oak season *to* treat him for oak, elm, maple, sycamore, *black walnut, etc., etc*, etc. You *might be sensitizing him* to elm and maple and the rest of them, when you only want to treat him for oak.

The same thing is true with mold extracts and it is a matter of great concern at the present time. Should you treat a patient with a mold mixture who reacts only to Alternaria? I don't think you should. The patient should be individualized. *Therefore, you would* make one emulsion for Bill Owen who is sensitive to three molds; a *different* one for Ken Craft who is sensitive *to two other* molds, and yet another for French Hansel who is sensitive only to Alternaria. In other words, regardless of whether you are treating these patients with emulsions or conventional multivisit type of treatment or with antihistamines or steroids or what, you have to individualize the patient you are treating. You can't treat the disease; you have to treat the patient

patient is bee-wasp sensitive other than to record the description of the attack in the history. The history is all-important for we cannot depend on the skin test reaction to bee-wasp or yellow jacket extracts, for diagnosis. If the patient shows a negative reaction, are you going to deny the fact that he is sensitive to the bee-wasp antigen? I'm not, I'm going to believe the history So, therefore, when a patient appears in my office and says he is sensitive to bee-wasp, I treat him with a dosage which I *think* he can tolerate.

One patient came in with a history of having been stung four times and on each occasion he thought he was dying. I made up a bee-wasp emulsion in the dosage that I thought would be satisfactory. The patient was given only 0 15 c.c. of this emulsion because I didn't want to risk a constitutional reaction He sat in my office for 1½ hours and he was fine, nothing happened Twenty minutes later his face was so swollen he couldn't see. I thought he was dying, and so did he Emergency procedures of epinephrine, intravenous steroid solutions, etc., were repeated for the next two hours until he was able to say. "That's exactly what I do when I get stung" *Do you know what he said* then? He said: "When do I come back for the next one? That was no worse than I have gone through with a sting and I want no more stings." He returned two weeks later and after preliminary protective epinephrine susphrine and steroids, he was given 0 85 c.c. of the same bee-wasp emulsion that had caused the reaction. He had no reaction this time. He has since been stung, with only a *local* reaction and this was no larger than the size of a lemon.

Of the patients who have been stung after receiving bee-wasp antigen, I can't think of a one who had more than local reaction. None of them had constitutional symptoms, at least none of those from whom I have heard.

QUESTION: You say that perfect emulsions are as safe as multiple dose injections?

DR. HALPIN: I think a perfect emulsion is *safer* than the average aqueous or glycerinated or multivisit type of injection because, if it is a perfect emulsion, nothing can happen. A patient on weekly injections has 52 chances each year to have a reaction; an emulsion patient has one. The emulsion cannot *now* be totally absorbed This droplet is broken up, that droplet is broken up and another and another in turn. The outer layer of droplets must be broken up before the next layer can be attacked, and so on to the next layer and the next layer, etc It is a slow prolonged type of absorption and that is why in a good emulsion there is little free antigen available to react on that patient now That answers the next part of the question which says, "What strength multiple dose injection do you mean, 0 1 c.c. of a 1-1,000,000 strength or of 1-100,000 or 1-10,000?" I don't think it makes any *difference because if the patient is going* to react to 1-1,000,000 or 1-100,000, he is going to react only because of the immediate absorption of that extract which was there for him to absorb and to which he would react.

If we lock the anigen inside a coating of oil, the antigen cannot be absorbed or released for a period of two or three weeks. This leaves little to which the patient can react. Let us say if an emulsion is 99% perfect, 1% is available to produce a reaction. But suppose the

scopic equipment. Small, air-cooled, high intensity mercury arcs housed in standard microscope lamp housings are available from several sources. Microscopes have been modified to permit easier observation as well as better photographic recording of the results. The basic equipment is now readily obtainable from several sources and is only moderately expensive.

Before considering some of the applications of fluorescent antibody technique, it is better to consider the method itself in order that some of the potential pitfalls may be understood and possibly avoided Several recent articles deal with various aspects of this technique (10, 11, 12, 13) No attempt will be made to review the vast literature that has now accumulated on fluorescence immunohistochemistry Rather, an attempt will be made to stress the general principles that are involved Reference will be made to review articles which have adequate bibliographies.

METHOD

Almost any microscope is satisfactory It should be equippel with a camera for permanently recording the results, and it should have a dark field condenser It is possible to obtain a black background using a bright field condenser with ultraviolet light However, the filter system required to remove all the visible light causes marked reduction in intensity of the ultraviolet light Therefore, a dark field condenser is usually more satisfactory The most convenient light source is an air-cooled, high pressure mercury arc Larger, water-cooled arcs give somewhat more intense illumination, but are rather cumbersome to use.

Since this method is an immunologic one, the results obtained depend largely on the quality of the antibody used. Commercially prepared antibodies are available from several sources However, each of these antibody solutions must be tested to evaluate the specificity of the antibody. It is best to separate the antibody fraction from the rest of the serum proteins. This can be accomplished either by ammonium sulphate fractionation or by the somewhat more complicated alcohol fractionation methods (12). If this is not done, there is greater likelihood of non-specific staining because of the presence of labeled proteins which are not antibodies

Once the antibody is obtained in a moderately pure form, it is a simple matter to conjugate it with the fluorescein isothiocyanate Dry powder is merely sprinkled into the buffered antibody solution (9) After a period of time, the noncoupled dye is removed by dialysis. However, there are troublesome, non-specific fluorescent products formed during the conjugation which are not removed by dialysis Hence, a further purification of the conjugated antibody is necessary. This can be accomplished in a variety of ways, including chemical precipitations of several sorts Most commonly, however, the labeled antibody solution is simply absorbed with acetone-dried liver powder after passing the conjugated antibody solution through a column of ion exchange resin (11). This treatment usually removes the materials which cause nonspecific fluorescent staining.

It is imperative to prepare the tissues or material which one wishes to examine in such a way that the immunological reactivity of its components is not destroyed The treatment which tissues can stand depends upon the materials for which one wishes to look Some substances such as pneumococcal polysaccharide remain active even in fixed blocks

USE OF FLUORESCENT ANTIBODY METHOD

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The application by Coons and co-workers of a method to couple a fluorescent compound to antibody made it possible to study histologically antigen-antibody interaction in tissues (1). Earlier attempts to do this, using antibody labeled with visible dyes, were generally not satisfactory because antibodies labeled in this way did not permit localization of small amounts of immunologically active materials (2, 3, 4).

Fluorescent compounds have the property of absorbing light energy of one wave length and emitting light of another wave length. By exciting fluorescent compounds with ultra-violet light it is possible to visualize them as a result of their emitted visible light It is easier to see objects appearing as bright areas against a dark background than it is to see darkly colored objects against an illuminated background. These are the reasons for the sensitivity of the method using antibodies labeled with fluorescent materials.

Later attempts to localize immune reactions in tissues using antibodies labeled with radioactive compounds were somewhat more successful (5, 6). Small amounts of immunologically active materials could be identified but the rather low resolution of these radioautographs did not permit precise localization of the sites of reaction.

The fluorescent antibody technique was originally described in 1942 (1) but it did not attract much attention until 1950 (7) when it was again described in a somewhat simplified form. However, even at that time, the method was so cumbersome that it was applied mainly in research centers. A complex organic chemical synthesis was necessary to prepare the fluorescein isocyanate for conjugation with the antibody In addition, this compound was very unstable. Carbon arc lamps were generally used as light sources. These were extremely hot and gave uneven, flickering light. High pressure, water-cooled mercury arc lamps were also available, but these were usually not supplied with suitable condensing lenses or housings.

There have been two major technical advances in recent years which have made it possible for an average laboratory to utilize this technique with a minimum of difficulty. Riggs and co-workers described the synthesis of fluorescein isothiocyanate, a chemical closely related to fluorescein isocyanate (8) This material is a stable compound which is now available commercially from several sources Conjugation with antibody is accomplished by merely sprinkling the dry powder into a buffered antibody solution (9). The second important factor has been the development of better micro-

Tissue antigens. Many studies have been concerned with the location of antigenic components in various tissues. The kidney, lung, and thyroid have been studied extensively. Systemic lupus erythematosus and the L. E. cell phenomenon have received considerable attention. Other human diseases including amyloidosis, glomerulonephritis, and rheumatic fever have also been investigated, using this method. Erythrocyte and platelet antigens, skeletal muscle fibers, the exocrine and endocrine portions of the pancreas, and the pituitary have also been studied. The results of these experiments have been reviewed in detail elsewhere (12).

Microorganisms. Most early studies of viral diseases using this technique were concerned with the pathogenesis of viral infections in experimental animals. The results of these studies have been thoroughly reviewed (12). Recently, largely through work at the Communicable Disease Center of the U.S. Public Health Service, the fluorescent antibody method has been extended to use in diagnostic virology, mycology, bacteriology, and parasitology. The fluorescent antibody test offers rapidity and considerable sensitivity in determining the presence of microbial agents in tissues and smears. It is possible to detect non-viable pathogens, and the presence of contaminating organisms does not interfere with the test. A major disadvantage of the test is the possibility of non-specific reactions. However, this is inherent in many situations using conventional diagnostic methods. Specific micro-organisms and details of the test used to identify each of these are outlined in a recent Public Health Service publication (13). While these tests have not all been thoroughly evaluated, it seems that the fluorescent antibody technique will soon be an accepted method in the diagnostic laboratory.

Allergic and hypersensitivity reactions: Although allergic and hypersensitivity reactions have an immunologic basis, they have been studied very little with the fluorescent antibody method. Much of the difficulty arises from the fact that many of the important hypersensitivity reactions are of a delayed type and apparently involve some sort of cellular antibody. This type of antibody has not been demonstrated using the fluorescent antibody method.

However, there are several types of allergic reactions that have been extensively studied. Dixon and his co-workers have examined experimental serum sickness in the rabbit (17, 18). They demonstrated that the specific antigen and host gamma globulin, presumably antibody, are localized in the lesions in the arterial wall.

The lesions develop at a time when soluble antigen-antibody complexes are present in the circulation. There is no detectable localization or fixation of antigen in those tissues which are predisposed to the development of serum sickness lesions before the lesions appear. The lesions regress after readily demonstrable antigen-antibody complexes disappear from the circulation. The regression of the lesions is associated with disappearance of antigen from them. The demonstration of these events was dependent largely upon the use of the fluorescent antibody technique.

The following sequence of events has been postulated (18). As antibody begins to be formed, it combines with the antigen in an antigen excess environment. Soluble complexes are formed in the circulation. These increase in amount until all

of tissues. In this case, paraffin sections can be prepared. In most instances, however, frozen sections of fresh tissues must be used. These are usually cut in a cryostat. This is a refrigerated box cooled to about –20°C in which the microtome is located. The sections are cut, transferred to a slide, thawed, and then fixed, if possible

Tissues containing many protein antigens can be fixed in ethanol without inactivating them. Most tissues infected with viruses must be fixed in acetone. Occasional substances are inactivated by any fixation and must be searched for in unfixed tissues. Freeze-drying and freeze-substitution have been used, but these techniques still introduce many problems.

To produce the antigen-antibody reaction in tissue sections, the slides are reacted with the labeled antibody solution, the excess unreacted antibody washed off, and the slide examined under ultraviolet light. Several controls are necessary to establish the specificity of the fluorescence which is seen. These include reaction of the section with unlabeled antibody to saturate the reactive sites followed by reaction with the labeled antibody. This should diminish or nearly abolish staining Preadsorption of the fluorescent antibody solution with the specific antigen should precipitate the specific labeled antibody or form soluble antigen-antibody complexes which would not react with the antigen in the tissues. This should abolish the fluorescence. A labeled, heterologous antibody should not stain the section. An unreacted section should not fluoresce. Occasionally other controls are used.

A valuable modification of this basic method is sometimes called the "sandwich technique." Using this modification, the tissue section is first reacted with specific, unlabeled antibody solution. This antibody, now bound to its specific antigen in the tissue, is visualized by reacting the section with a labeled antibody directed toward the unlabeled antibody. For example, it is possible to localize some viruses in human tissues by treating tissue sections with convalescent serum followed by reaction with a labeled anti-human globulin solution. This modification permits one labeled antibody solution to be used to demonstrate the reactions of several antigen-antibody systems It is frequently more sensitive. Also, antibody can be demonstrated in tissue sections using the specific antigen as the middle layer and the labeled antibody as the final layer. However, the "sandwich technique" requires more controls to prove the specificity of the reaction.

Fluorescein is the dye usually used for conjugation. There are several reasons for this. It is a very efficient fluorescent material, converting a large proportion of the absorbed energy into visible light The yellow-green fluorescence is in the range of light to which the human eye is most sensitive Also, this color is seldom seen in the autofluorescence of tissues. Occasionally, it is desirable to label antibody with a fluorescent dye of another color. Several are available; of these, rhodamine, a red dye, is most frequently used (14, 15)

APPLICATIONS

Most of the early applications of this method were directed toward basic immunologic problems. The distribution of various antigens was determined (2, 10). The cellular changes occurring during antibody formation were studied (10, 16). As the potential of the technique was recognized, many other areas were explored.

sponse of the host to this reaction? Answers to these questions should give a better understanding of the pathogenesis of these allergic conditions and may offer a clue to more rational therapy.

SUMMARY

The fluorescent antibody technique offers a sensitive method to study the precise *localization of antigen-antibody* reactions in tissues The serological specificity of this method allows it to be applied also to the rapid diagnosis of microbial agents in biological materials The method is now sufficiently simple and good equipment has become so readily available that it is possible for most laboratories to apply the technique with minimal difficulty.

The pathogenesis of experimental serum sickness, the Arthus reaction, and anaphylaxis in the rabbit have been partially clarified through the application of this technique Studies have been performed on the wheal reaction in human patients sensitive to egg white. Many clinical and experimental allergic and hypersensitive conditions appear to have as their basis the reaction of humoral antibody with antigen Study of these conditions by the fluorescent antibody method should furnish considerable basic information about their pathogenesis and may suggest a basis for more rational therapy

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of the antigen is eliminated. These soluble complexes circulate in the blood stream and by means not yet known, initiate and are localized in allergic, inflammatory lesions in certain arteries and glomeruli. As the complexes are eliminated from the circulation, the lesions of serum sickness promptly burn themselves out and are repaired.

The events taking place in the Arthus type of hypersensitivity lesion have been studied by Cochrane and Weigle (19), and by Cochrane, Weigle and Dixon (20). In both the active Arthus reaction and the reverse passive Arthus reaction, antigen and in all likelihood, antibody, became localized beneath the endothelial cells to form a deposit within the vessel wall. If the experimental animal was depleted of polymorphonuclear leukocytes before the challenge injection, there was no vascular inflammation or necrosis in response to the antigen-antibody complex. In normal animals, polymorphonuclear leukocytes accumulated and inflammation was prominent. The mechanism by which the polymorphonuclear leukocytes were instrumental in producing the inflammatory angiitis in the presence of antigen and antibody is not clear. It does appear, however, that the antigen-antibody complexes do not cause the inflammation without the participation of other factors.

Large amounts of antigen and antibody are required to produce anaphylactic shock in the rabbit. McKinnon *et al* (21) using rabbits sensitized with bovine serum albumin demonstrated intravascular precipitation of antigen with antibody *in vivo* after injection of fluorescein-labeled antigen. They suggested that obstruction of pulmonary capillaries by immune precipitates was an important mechanism in the pathogenesis of anaphylactic shock in the rabbit.

Few studies have utilized human allergic tissues. Pioneering work has been done by Rappaport who has studied the wheal reaction in human volunteers with a clinical sensitivity to hen's egg albumin (22). Biopsies were performed on unchallenged skin, on the wheal site after a scratch test with egg albumin, and on the wheal site after a screatch test with histamine. Sections of the skin were treated with fluorescein-labeled globulin fractions obtained from serum of the patients who had volunteered for the skin biopsies. The fluorescein conjugation had little effect on the ability of this serum to confer passive sensitization to non-allergic individuals.

In the site challenged with egg albumin, the epithelial cells of the epidermis, sweat glands, hair follicles and sebaceous glands gave specific staining for the egg albumin. In addition, intense staining was present in macrophages and pericapillary cells. The endothelium of small blood vessels stained less intensely, but fibrous tissue bundles were specifically stained. The histamine wheal and normal skin did not stain with the labeled antibody.

It is evident that only a beginning has been made in the study of allergic reactions by means of the fluorescent antibody method. Many problems of allergy and hypersensitivity can be examined profitably by using this method. What is the pattern of reaction of antigen and antibody in nasal mucosa? What is the localization of soluble antigen-antibody complexes injected by various routes into different species of animals? What is the role played by blocking antibody in allergic reactions? What are the effects of anti-inflammatory steroids and antihistamines on the localization of the antigen-antibody reaction and the re-

THE USE OF CORTICOSTEROIDS IN ALLERGIC DISEASE OF THE EAR, NOSE AND THROAT

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Since basically disease is the result of reaction of the individual cells to environmental influences, it seems logical to review allergy, which is essentially a form of inflammation, in the light of connective tissue responses This is especially timely because of the progress made in the study of connective tissue in the past decade

Connective tissue consists of an aggregation of cells and elastic and collagen fibers in a surrounding matrix, the ground substance The commonest cell is the fibroblast, which constitutes about ninety percent of the connective tissue cells It produces mucopolysaccharides which intersperse between the scaffolding of connective tissue to form the ground substance.

The second cell is the histiocyte or macrophage, a primitive, reticulo-endothelial cell, which are the scavengers of this area These cells wander throughout the ground substance, clearing debris Their activity is markedly influenced by the predominant material in the surrounding ground substance. Histamine slows their activity tremendously while heparin activates the engulfing of particles.

Although polymorphonuclear cells are not present in connective tissue, inflammation brings out all of the white blood cells The polymorphonuclear leukocytes have an affinity for clearing away bacteria. The lymphocytes also help clear infection by transformation to macrophages They also have the further function of producing antibodies and perhaps other constituents of gammaglobulin. It should be noted that corticosteroids destroy lymphocytes, and suppress their entrance into inflammed areas. Thus at times of stress, a change occurs in their cytoplasm, so that they may be easily recognized as stress lymphocytes The role of the eosinophil is not known They have been thought to transport histamine, but do not always contain this substance. One constituent is the basic protein molecule, spermine, but its function is unknown There is evidence that the eosinophils may aid the phagocytosis of dead cells that macrophages are unable to fracture and engulf These cells are tangentially contacted by eosinophils which produce some unknown alteration in them The only mechanism that can be seen is a whirling motion of nucleoli, as of a bucket brigade. After some time, the eosinophils break contact with the dead cells and wander off Macrophages then return and are able to break down the cells and ingest this cellular debris.

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ment is not of great use in allergy, for those studying otosclerosis it may be of extreme interest At present, our energies are being expended to produce bypass mechanisms around the ossicular tumor Eventually, it will be necessary to discover how the ground substance calcifies the fibrous tissue, and why it does this in otosclerosis; then we may be able to eliminate the disease instead of merely eliminating the deafness, temporarily

Intertwined between the cellular elements and the ground substance in connective tissue, are elastic and collagen fibers These fibers are created by the *fibroblasts* *The collagen* fibers particularly, are extremely interesting in that they have a definite spatial relationship. If they are stretched until this spatial arrangement is broken, disease is produced Progress is being made in studying these linkages in the hope that their changes may give information of use in controlling the collagen diseases

Finally connective tissue does a great deal to maintain the milieu internale by establishing ion exchange mechanisms in the ground substance. Through this mechanism, either acid or alkaline material may be bound At present, it is believed that inflammation occurs because of the presence of catechol amines liberated when any type of tissue damage occurs These amines are detoxified in connective tissue As noted earlier, when histamine is liberated in the neighborhood of a mast cell, its contained granules explode, liberating histamine and heparin The histamine, being a small molecule, enters the capillary best through the ground substance barrier and diffuses throughout the body, while the heparin unites with the neighboring histamine, neutralizing it. Being a larger molecule, it can enter the blood stream only via the lymphatics; hence these salts again form small granules which are picked up by fibroblasts, turning into mast cells.

Before leaving connective tissue and its functions, it may be advantageous to stress that this is not a static area, but one of constant motion. Gels are continuously turning to solids, and vice versa as the ground substance changes. The changes are local; they may be turning to gel at one point, and a few centimeters away may become liquid. The local situation depends on the degree of polymerization. Throughout this apparent jungle of ground substance and intertwined collagen and elastic tissues, one finds cells wandering about. It is interesting to speculate that each cell seems to have a specific function. If bacteria are present, polymorphonuclear cells will invade and engulf them. The polymorphonuclear cells will not touch cellular debris, which is picked up by the macrophages. The little granules of debris are picked up by fibroblasts and form mast cells, which disintegrate as mentioned when damage is done to the area The activity varies with pH. If histamine is liberated, the tissue swells and cellular activity decreases, especially scavenging The mast cells then degranulate and decompose This arrests the swelling and reactivates the macrophages If heparin is added, the activity is tremendously enhanced and soon the area is clean and normally active.

It has been shown repeatedly that any type of injury (thermal, chemical, bacterial or physical, etc) causes the liberation of histamine, or the H substance of Lewis. His wisdom in calling the inflammatory agent "H" substance, though he was quite sure it was histamine,

The function of the plasma cell is also in doubt. Many claim it produces antibody protein, as gammaglobulin; others doubt this. Further study will be necessary to determine the correct answer. Mast cells are also present in large numbers While it is classified as a distinct cell, it is our feeling that the mast cell most probably represents a fibroblast which has picked up metachromatic granules, which are probably the salt formed by the union of histamine and heparin. This salt is then metabolized and histamine and heparin are held in readiness *for extrusion from the cell.*

The primitive one-celled animal required a semi-permeable membrane that could contain the cell, allow it to extract nourishment from the surrounding area and to excrete waste products. This was the beginning of the ground substance.

Phylogenetically, animals are not the only ones that have developed a ground substance. Plants have small hollows, called canaliculi, which run the length of the plant. These canaliculi are filled with polymers of the sugar, xylose. This sugar enables the tree to extract water and various salts from the earth and transport them to the ends of the tree for nourishment. Waste products are eliminated *in the opposite direction*

In animals, instead of xylose, glucose and galactose serve as the basis of the mucopolysaccharides that form their ground substance. Without this ground substance, neither the trees nor the animals could have developed into a multicellular animal. A unicellular animal has no difficulty in extracting nutrients from the surrounding water, and excreting wastes. Multicellular animals, however, had to develop some way of binding the cells together. The ground substance has served as a mortar, forming one animal and yet, at the same time, allowing each cell to selectively allow material to pass within the cell or to be excluded Were it not for this ground substance, each cell would have to remain similar, and development would have been restricted to forms similar to the sponges. It has further allowed us to develop specificity in cells and yet exchange material throughout all of them.

As animals developed phylogenetically and locomotion increased, a circulatory system developed which could carry metabolites throughout the body. However, *it must be noted that after leaving the* capillaries, the metabolites must traverse the ground substance in order to enter the individual cell, where final metabolism occurs. The ground substance is the final guard, allowing the entrance or exit of any material into, or from, the cells.

As mentioned, ground substance consists of polymers of the two sugars. As the polymerization increases, the number of free bonds decreases Therefore, an individual who is edematous finds it easier to exchange ions than one in whom polymerization has occurred until there are few free bonds The practical application of this is to point out that if too much water is extracted, it becomes dif*ficult for ions to reach the cells to bring* the materials needed for metabolism.

This action of ground substance is enhanced by the action of hyaluronidase, which increases permeability of membranes. This allows larger molecules to reach many cells more easily and even to cross the capillary barrier.

Another function of connective tissue is to give rigidity and strength to the framework of the body. Bones are actually a form of ground substance in which the fibrous tissue has become calcified. While the importance of this at the mo-

throughout the body. Therefore, one must be certain which organism is infecting the body and, further, certain that one can control it with either a chemotherapeutic or antibiotic agent in order to prevent the infection's spread. If one does not have such control of infection, it is better not to use the adrenal extracts.

Thirdly, cortisone has been found to decalcify bones through allowing the escape of calcium If used too long, one may have the difficulty of pathologic fractures. In a few cases, cortisone also affects other ductless glands, particularly the pancreas to produce diabetes. It is our feeling that the thyroid also probably is affected. The degree has not yet been measured At the moment, extracapsular cataracts are produced by the use of steroids These are so well known that one need not discuss them.

While the steroids are dangerous, if used properly in small, non-continuous bursts they are of great help in hay fever, urticaria, hives, sinusitis and polyp formation. By decreasing the ground substance they decrease the edema, and hence the size of the turbinates and the polyps Histamine spreads through the body more slowly and the allergy is more easily controlled While the loss of inflammation is a danger in the presence of infection, if infection is controlled by antibiotics the shrinkage of the nasal tissue affords both symptomatic improvement and lessening of the histamine producing the allergy

apparent, for we are finding that not only histamine, but many amines, as serotonin, carnesine, etc., all act in the same way.

Drs. Eyring and Dougherty have postulated that sodium or potassium may be transported by a chelation process, using histamine, across the fibroblast's membrane. The basic idea of chelation is that ions produce a voltage difference across a cell membrane and thus electrically transport molecules. The mechanism differs from the formation of the usual covalent bond in that the metal ion does not share its electrons, but is held by a force of attraction, and thus the chelator can move the ion without being chemically changed. *It is felt that the mechanism by which inflammation is produced is fundamentally due to the enhanced transport of sodium across the fibrous membrane.* The sodium is accompanied by molecules of water across the membrane into the cell In time, the accumulation of water causes the fibroblast to swell and finally to break. This releases the histamine complex, which is still chemically unchanged and thus able to attack the remaining cells Thus each cell broken down actually promotes the destruction of neighboring cells, and a chain reaction of destruction results Death would always be the end result if the body were not able to control inflammation. This is easily seen in an adrenalectomized animal as inflammation will often set up a chain reaction resulting in death.

In the average animal, the chain reaction is controlled by three mechanisms. First is the excretion of histamine. This was demonstrated by Bram Rose in a most ingenious experiment. He gave ACTH to patients with known allergy to ragweed several days before the plants pollenated. He was thus able to show that he could control the hay fever sensitivity but that histamine would be secreted in the urine as soon as the pollen appeared. The second mechanism is local detoxification which we have just been discussing. The third is the action of the steroids.

The steroids decrease production of ground substance in hyaluronidase and thus tend to limit the spread of the histamine. A much stronger mechanism, however, occurs through the action of cortisol, which is picked up by the fibroblasts and toughens their cell membranes against histamine's transport of sodium into the cell. Thus the chain reaction is arrested.

The difference in action between the steroids and heparin should be noted By understanding these actions we are no longer limited to the steroids but have a new mechanism available to us for the control of allergies.

When the action of the adrenals on allergy was first discovered, it was felt that a control was now available for this disease Unfortunately, its use as a drug demonstrated that it is not without dangers The use of cortisone decreases the activity of the adrenal glands, and when the patient faces a stress, the glands may not be able to produce sufficient hormone to cover the period of shock. This is extremely important to remember, for should a patient require surgery after having cortisone, or be put through a series of stresses, it is extremely important that additional cortisone be added to supplement that which the body can produce, otherwise death by shock may result.

Further, it has been found that through the reduction of inflammation, cortisone will permit infections to spread rapidly

throughout the body Therefore, one must be certain which organism is infecting the body and, further, certain that one can control it with either a chemotherapeutic or antibiotic agent in order to prevent the infection's spread. If one does not have such control of infection, it is better not to use the adrenal extracts.

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THE DIAGNOSIS AND MANAGEMENT OF NON-GRANULOMATOUS UVEITIS

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I would like to discuss the diagnosis and management of uveitis under four subheadings. classification, pathogensis, diagnostic procedures and management. I think the last two depend upon classification and pathogenesis, and for that reason I will start by discussing, briefly, the classification of uveitis

The most important advance in this field was made in 1947 when Woods subdivided uveitis into non-granulomatous and granulomatous uveitis, which he based upon the different pathological pictures found in enucleated eyes. He called the first type non-granulomatous uveitis, and a picture of this condition taken from Woods' book shows intense cellular infiltration with lymphocytes, plasma cells and monocytes. Woods considers this type of reaction to be primarily of the allergic variety. He considers the second type to be due to organismal invasion which gives rise to a specific reaction termed the granulomatous reaction. This is characterized by giant cell 'formation, epithelial cells, plasma cells and lymphocytes which give rise to the characteristic granulomatous picture.

Woods' contribution to the classification of uveitis is a landmark. However, certain valid criticisms of it can be made. These criticisms can be made on clinical grounds, on pathological grounds, and on immunological grounds

First, in terms of the clinical grounds, I frequently find it very difficult to notice any difference between the non-granulomatous and the granulomatous states As far as I am concerned, one will merge imperceptibly into the other. I have often seen patients who had non-granulomatous uveitis, but when I looked in a week later, it was a typical picture of granulomatous uveitis, and vice versa. I have almost come to the conclusion that the difference is one of degree due to the insult to the ocular tissues, which results, let us say, in a greater outpouring of epitheloid cells and the formation of these large mutton-fat precipitates. In leptospirosis where actual organismal invasion of the eye occurs, we have a typical non-granulomatous picture. And in two of the prime allergic diseases of the eye, namely, endophthalmitis phakoanaphylactica and sympathetic ophthalmia, which undoubtedly are diseases of a hypersensitive nature, the clinical picture is typical of the granulomatous reaction with lardaceous, heavy, mutton-fat K.P's, low grade flare and characteristic morphologic changes. And so, clinically, this classification leaves us in doubt.

Pathologically, it can be criticized as well. Ashton has pointed out that the term "granulomatous reaction" merely applies to those chronic inflammatory reactions which occur over a prolonged period of time since any protracted infection will develop the characteristic picture of a granulomatous reaction, with or without actual organismal invasion, if long enough in duration. Also, inert substance can give the typical granulomatous picture. For example, wood, beryllium, silica, talc, etc., give beautiful granulomas when the eye is examined, histologically. And lastly, Frenkel and Jacobs have shown that in the organismal invasion which occurs in toxoplasmosis, there is absolutely no tendency for granulomas to form.

Immunologically, also, this classification can be criticized. Rich believes that it is possible to get the typical granulomatous picture in the eye, as elsewhere in the body, purely on the basis of an antigen-antibody reaction. In other words, to get this definite granulomatous picture, organismal invasion is not required. All that is needed is antigen and antibody. A slide of the spleen of a patient who had a fatal hypersensitive reaction to iodine showed a typical granulomatous picture. And another slide showed giant cells which formed in the spleen of a rabbit treated with serum sickness type of antigen-antibody reaction. Goldgraber and Krismer have stated that the pathological occurrence of granulomata is evidence per se of a hypersensitive state.

We do not feel that it is possible to classify uveitis solely as granulomatous or non-granulomatous. At the New York University-Bellevue Medical Center we have developed the habit of classifying uveitis in the simplest fashion, namely, whether it is anterior or posterior uveitis, panuveitis, acute or chronic, and then we give it a secondary, morphological classification; we state whether or not it is of the non-granulomatous or the granulomatous variety.

The following table outlines the major pathogenic mechanisms which exist in uveitis.

TABLE I

PATHOGENESIS

1 FOCI OF INFECTION
2 DIRECT ORGANISMAL INVASION
   a. Bacteria
   b. Viruses
   c. Spirochetosis
      Treponima pallidum
      Leptospirosis
   d. Protozoa
      Toxoplasma
      Parasitic diseases
   e. Fungus infections
3 HYPERSENSITIVITY
4 SYSTEMIC DISEASES

Regarding foci of infection, it seems regrettable to me that it is only in ophthalmology that we still find adherence to the concept of foci of infection. I think every other major branch of medicine has more or less discarded this con-

cept, including the rheumatologists, who at one time looked for foci of infection in seeking the cause of arthritis. In our experience, we have not had too much success in curing uvetis by eliminating foci of infection. However, I must give you the other side of the coin. There are many people who believe very strongly in foci of infection and I respect their opinion. Halland and Whorlton, for example, recently have claimed that chronic genitourinary tract infections are associated with a pleuro-pneumonia type of organism and give rise to an anterior type of uveitis. They claimed considerable improvement of the uveitis coincident with clearing of the G. U. infection with oxytetracyline. Cattarall, in England, found a high incidence of genitourinary tract infections but, on the other hand, he was unable to alter the uveitis by controlling the G. U. pathology. Castroviejo feels very strongly that patients with keratitis and uveitis respond well when their foci are removed. However, I have lots of good company, Hogan, Kimura, and Thygesen in San Francisco, have completely given up the search for foci of infection Schlaegel also has been rather doubtful of any good coming from the elimination of foci of infection. Also, Bennett, in England, states that the English probably have the worst teeth in the world, yet the incidence of uveitis among them is no higher than in any other group I have spoken to many oculists who told me that they did have patients whose uveitis improved after tonsillectomy, but I have not been able to track one down. In France, Offret and Sarraut feel that 35% of all anterior uveitis is due to foci of infection located in the paranasal sinuses. However, in a large series of patients, they were able to recover microorganisms which were similar only on two occasions—similar, i.e., in the eye and in the sinuses. As far as I am concerned, the concept of foci of infection is not very tenable.

The next possibility is that of direct organismal invasion causing uveitis. In this country all attempts to isolate bacteria from the anterior chamber during the height of the uveal attack, anterior or posterior, have been unrewarding. Von Sallmann, Brown and many others, including ourselves, have never recovered any organisms from the aqueous. In Europe, reports of recovering organisms, most commonly nonpathogenic staphylococci, are frequent. However, if staph or strep organismal invasion did play a role in the causation of anterior uveitis, we would expect purulent reactions, certainly so with the more pathogenic ones. Lastly, we would expect the uveitis to be aided by antibiotics, which it isn't

A considerable amount of work has been done in recent years on viruses, although it has been shown definitely that no virus exists with a specific trophism for the uveal tract. In the literature, I have come across only two reported isolations of viruses from the aqueous during the course of anterior uveitis. Both reports were of the isolation of herpes simplex virus At the Proctor Foundation much virus study has been performed Thygeson, Kimura and Hogan report that three days after the injection of viruses into the anterior chamber in animals, that it is impossible to recover them. It may be that virus isolation techniques have been inadequate. Now, this may be because, as you know, the virus is an obligatory intracellular parasite and needs cells to live on, and usually only aqueous is aspirated. Perhaps if we could aspirate a little bit of the iris at the

same time, we would find virus But even though viruses have not been isolated from the anterior chamber I think that they do play an important role in the causation of uveitis I think they do it secondarily; I think it is secondary to virus infection elsewhere in the body which manifests itself in the eye.

The most important protozoon in the causation of uveitis is the toxoplasma This organism has been recovered frequently and Table II shows the number of times that toxoplasma has been recovered from the human eye.

TABLE II

RECOVERY OF TOXOPLASMA FROM HUMAN EYES

Author	Sex and Age	Duration	Type	Ant vs Post.	Eye Involved	Skull X ray	Dye Titer		Virulence
							Before	After	
Jacobs, L., Fair, J., Bickerton, J., 1954[69]	Male, 30 yrs	8½ yrs	Acquired	Post	O S.	Neg	1.64	1 wk 1 4096 2 wks 1 128	High
Habegger, 1954[73]	Male, 2 mos	Since birth	Congenital	Post	O D	Hydrocephalic	1 6000		?
	Female, 45 yrs	?	Congenital	Post	O D—new O S—old	Neg.	1.2048	1 16000	High
Hogan, M J., Zweigart, P., Lewis A., 1958[66]	Male, 20 yrs	8 yrs	Congenital	Post	O D—old healed central C R O S—Active lesion	Pos.	1 128	1 16	Low
Pillat, Thalhammer 1957[109]	Male, 11 yrs	3 mos (?)	?	Ant	O U	?	1 16384	1 256	?

In regard to fungi, there is a great deal of interest which has been aroused by Dr. Alan C Woods in a recent paper on histoplasmosis in which he postulated that histoplasmosis is a possible common cause of uveitis I haven't had any experience with histoplasmosis as a cause of uveitis and I must confess that I find it a little bit difficult to accept this as a cause of chronic uveitis The only histoplasmosis I have seen is as a *systemic* disease, and these are sick people.

Our next pathogenetic mechanism is most important, hypersensitivity. Table III shows a classification of hypersensitivity as it may be responsible for uveitis

TABLE III

CLASSIFICATION OF ALLERGY OF THE UVEA

1. ANAPHYLACTIC AND ATOPIC REACTIONS

2. [illegible] nature

3. [illegible] is, lues, toxoplasmosis, brucellosis

[illegible] nous uveal pigment)

[illegible] to autogenous lens protein)

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Our next pathogenetic mechanism is most important, hypersensitivity Table III shows a classification of hypersensitivity as it may be responsible for uveitis.

TABLE III

CLASSIFICATION OF ALLERGY OF THE UVEA

1. ANAPHYLACTIC AND ATOPIC REACTIONS
   Uveitis from Sera, pollens, animal proteins, foods, drugs, angioneurotic edema
2. MICROBIALLERGIC REACTIONS
   a. [illegible] strepto-
   [illegible]
   b. [illegible] may alter the nature
   (inflammatory response) tuberculosis, lues, toxoplasmosis, brucellosis
3. AUTO[illegible]
   a. [illegible] nous uveal pigment)
   b. [illegible] to autogenous lens protein)

The first group, anaphylactic and atopic reactions of the uvea, definitely occurs. Uveitis may also be due to pollen, and I have now collected six instances from the literature. In addition, while discussing pollens with Dr. Prewitt, he mentioned a patient whose uveitis was directly associated with a specific pollen. An interesting instance is reported by Walker of a woman who had a severe anterior uveitis and who finally had to be hospitalized. When she entered the hospital her uveitis cleared dramatically, only to recur when she went home. Further investigation revealed that she had a pet cat at home and that she was highly sensitive to cat dander They took away her cat and her uveitis cleared up. Under the second category of microbiallergic reactions, allergy is apparently the main factor.

Currently, there is a belief that the streptococcus plays a very important role in the causation of uveitis. We ran a large series of serial antistreptolysin titers in patients with uveitis and in a control group In this study we could find no correlation between serologic evidence of streptococcal disease and the presence of uveitis. We do not feel that the streptococcus is an important factor in the causation of uveitis.

Tuberculosis had a tremendous vogue in the past as a cause of uveitis, but the "therapeutic test" for tuberculosis has shown that tuberculosis is not as common in uveitis as it was originally thought to be. However, the fact that tubercle bacilli can give rise to allergic reactions is intriguing and I think that some anterior uveitis may conceivably be hypersensitivity to the tubercle bacillus. I might add that skin tests revealed a higher incidence of positive reaction to tuberculin in patients with anterior uveitis than in those with posterior uveitis.

I would like to discuss autogenous allergic reactions. I think the best examples of these are sympathetic ophthalmia and endophthalmitis anaphylactica. I think that analysis of what is known about sympathetic ophthalmia leads to the realization that this is primarily a hypersensitive disease. Ever since Elschnig proposed, in 1910, that uveal pigment was a cause of sympathetic ophthalmia, evidence has accumulated to buttress this concept. In the twenties, Friedenwald developed a skin test employing uveal pigment, which he found was positive only in patients with sympathetic ophthalmia Woods isolated a specific antibody in patients with sympathetic ophthalmia While there is much that we don't know about sympathetic ophthalmia, most of the evidence would indicate that this is a reaction of hypersensitivity, perhaps triggered by some low grade infection or conjunctivial saprophyte.

Endophthalmitis anaphylactica is of a similar nature, I think In this instance, the lens is the antigenic substance Witmer has skin tested these patients and he has also done antibody studies on the aqueous and he has found that these patients do have specific antibodies to their own lens protein So I think this comes into the category of an allergic mechanism I think basically, as we go down the line even in the large group of nonspecific uveitides, that eventually we may find that these represent autoallergy to uveal pigment. Possibly an antigen unites with the mucopolysaccharides of the uveal tract, forms a hapten-like complex which then leads to autosensitization, with recurrent bouts of uveitis.

In any search for causative agents in uveitis it soon becomes apparent that there is a large number of systemic diseases which are associated with uveitis I would like to briefly discuss some of these systemic diseases and their uveal manifestations. I have listed them in Table IV.

TABLE IV

SYSTEMIC DISEASES ASSOCIATED WITH UVEITIS

RHEUMATIC DISEASES
SARCOIDOSIS
SPIROCHETOSIS
A. Syphilis
B. Leptospirosis
VIRUS DISEASES
TUBERCULOSIS
TOXOPLASMOSIS
TROPICAL DISEASES
PSYCHOSOMATIC FACTORS

I have excluded all of the degenerative conditions, such as osteoarthritis, which are not associated with uveitis. Approximately 2% to 5% of patients with rheumatoid arthritis will develop anterior uveitis. The average time for development usually is from two to four years, although it sometimes takes twelve years until uveitis becomes manifest. Uveitis associated with rheumatoid arthritis can manifest itself in two different patterns The first type can appear as a unilateral, acute, anterior uveitis which recurs over a period of years, usually associated with very fine thin K Ps, intense aqueous flare and many cells of the lymphoid type in the anterior chamber This type usually gets better with or without treatment in about 4 to 6 weeks and usually causes no damage with the initial attack It is only as a result of repeated attacks that synechiae and other permanent changes appear which lead to irreversible damage Frequently, changes in the posterior segment occur, such as edema of the macula and occasionally a papillitis. This type of uveitis is unrelated to the severity of rheumatoid arthritis Any visual loss which occurs is due only to the changes occurring in the anterior segment. The second type of uveitis found with rheumatoid arthritis is a slow torpid, smoldering uveitis which is unresponsive to all types of therapy and can eventually lead to cataracts, phthisis bulbi or secondary glaucoma This second variety seems to be very closely associated, I find, with the more severe type of joint manifestations.

The juvenile form of rheumatoid arthritis is a fulminating disease. These children usually come down with hepatosplenomegaly, severe joint manifestations and high fever They are very sick children Occasionally they present a severe uveitis, and later develop the typical classical picture of juvenile rheumatoid arthritis We have seen this in two patients In these patients, tests to determine the presence of the rheumatoid factor are positive.

The second rheumatic disease of importance in uveitis is ankylosing spondylitis This is a completely different disease from rheumatoid arthritis although in the past they were considered somewhat similar. The incidence of uveitis in ankylosing spondylitis is, of course,

The *first group, anaphylactic and* atopic reactions of the uvea, definitely occurs. Uveitis may also be due to pollen, and I have now collected six instances from the literature. In addition, while discussing pollens with Dr. Prewitt, he mentioned a patient whose uveitis was directly associated with a specific pollen. An interesting instance is reported by Walker of a woman who had a severe anterior uveitis and who finally *had to be hospitalized. When she en*tered the hospital her uveitis cleared *dramatically, only to recur when she* went home Further investigation revealed that she had a pet cat at home and that she was highly sensitive to cat dander. They took away her cat and her uveitis cleared up. Under the second category of microbiallergic reactions, allergy is apparently the main factor.

Currently, there is a belief that the streptococcus plays a very important role in the causation of uveitis. We ran a large series of serial antistreptolysin titers in patients with uveitis and in a control group. In this study we could find no correlation between serologic evidence of *streptococcal disease and the* presence of uveitis. We do not feel that *the streptococcus is an important* factor in the causation of uveitis.

Tuberculosis *had* a tremendous vogue in the past as a cause of uveitis, but the "therapeutic *test*" *for tuberculosis* has shown that tuberculosis is not as common in uveitis as it was originally thought to be. However, the fact that tubercle bacilli can give rise to allergic reactions is intriguing and I think that some anterior uveitis may conceivably be hypersensitivity to the tubercle *bacillus. I* might add that skin tests revealed a higher incidence of positive *reaction to tuberculin in patients with anterior* uveitis than in those with posterior uveitis.

I would like to discuss autogenous allergic reactions. I think the best examples of these are sympathetic ophthalmia and endophthalmitis anaphylactica. *I think that analysis of what is known* about sympathetic ophthalmia leads to the realization that this is *primarily a* hypersensitive disease. Ever since Elschnig proposed, in 1910, that uveal pigment was a cause of sympathetic ophthalmia, evidence has accumulated to buttress this concept In the twenties, Friedenwald developed a skin test employing uveal pigment, which he found was positive only in patients with sympathetic *ophthalmia Woods isolated a specific* antibody in patients with sympathetic *ophthalmia. While there is much that* we don't know about sympathetic ophthalmia, most of the evidence would indicate that this is a reaction of hypersensitivity, perhaps triggered by some low grade infection or conjunctival saprophyte

Endophthalmitis anaphylactica is of a similar nature, I think. In this instance, the lens is the antigenic substance. Witmer has skin tested these patients and he has also done antibody studies on the aqueous and he has found that these *patients do have specific antibodies to their* own lens protein So I think this comes *into the category* of an allergic mechanism. *I think* basically, as we go down the line even in the large group of nonspecific uveitides, that eventually we may find that these represent autoallergy to uveal pigment. Possibly an antigen unites with the mucopolysaccharides of the *uveal tract, forms a hapten-like complex* which then leads to autosensitiza*tion, with recurrent* bouts of uveitis.

LABORATORY FINDINGS:
- Increased serum Globulins (A/G Reversal)
- High Ca^{++}, Low P^{+}
- Sedimentation rate
- Radiographic findings
- Nickerson-Kviem test positive 85%
- Positive Biopsy

One of the common causes of uveitis, especially in Negroes, is sarcoid. Uveitis comprises 55% to 60% of all ocular involvements in sarcoid, and uveitis in sarcoid is wicked. Usually the onset is gradual although sometimes there are acute episodes. These patients develop iris nodules, rapid formation of synechiae and very large mutton fat K.Ps., which appear in triangular formation on the bottom of the cornea. Large cells are seen in a very slow convection current, and despite intensive therapy severe posterior synechiae develop. Many peripheral anterior synechiae also appear. I am certain that the tendency to synechiae formation in these patients is related to the change in the systemic albumin-globulin ratio which they have. All too frequently these patients will do extremely poorly despite intensive therapy with local and systemic steroids and mydriatics. The prognosis can be extremely bleak in this disease. One aspect which has not been emphasized enough in the literature is that not only does sarcoid affect the anterior segment but there are often marked fundus changes as well. The veins exhibit sheathing, tortuosity and segmentation. They seem engorged and full and "tallow spots" appear alongside them. These were first described by Franchischetti, who so named them.

I think we need not dwell too long on spirochetosis. Although syphilis can cause uveitis, it is not a common cause. We have had quite a few positive serologies but none which we felt was related to the uveitis.

Leptospirosis, however, is a cause of uveitis but should be suspected only when there is a history of exposure, such as in laboratory workers. The ocular manifestations usually appear from four to six months after the disease has been contracted, although they do occur as early as two weeks or as late as eighteen months afterward. Approximately 10% to 44% of the patients with leptospirosis develop anterior uveitis, resulting in a low grade, chronic condition. The patient whom I saw was a young resident in surgery. He was a Swiss boy who had been working with rats in Zurich when he developed leptospirosis. Six months later, during his surgical residency at our hospital in New York, he developed a mild anterior uveitis, with not too much flare but with a red eye and much photophobia. In the course of one year, a mature cataract appeared in the affected eye. He also developed an acute glaucoma which we thought was due to steroids. Following cataract extraction, his condition became quiescent.

TABLE VII

VIRUS UVEITIS

I. ASSOCIATED WITH SYSTEMIC VIRUS DISEASES
   a. Influenza
   b. Exanthemata
   c. Mumps
   d. Infectious Mononucleosis and Hepatitis

much higher than in any of the other rheumatic diseases. *The incidence is reported to be 8% to 20%*, although Vesterdal states that 30% of patients with ankylosing spondylitis will have anterior uveitis. Laitenen, in Finland, studied a group of patients with anterior non-granulomatous uveitis and found that 30% of these patients had undiagnosed ankylosing spondylitis, discovered in x-rays of the lumbo-sacral region. I believe ankylosing spondylitis is quite common, *and since we have a large arthritis clinic at Bellevue hospital, I see it fairly frequently.* Ankylosing spondylitis occurs mostly in patients from twenty to forty years old. If a patient in that age group presents with an anterior uveitis, I think we should question him very thoroughly as to the presence of low back pain. We should also get x-rays of the lumbo-sacral spine, since frequently ankylosing spondylitis is not clinically manifest; we have to elicit it; we have to find it.

TABLE V

RHEUMATIC DISEASES

1. RHEUMATOID ARTHRITIS (R. F. present)
   - Adult form
   - Juvenile form (Still's disease)
2. ANKYLOSING SPONDYLITIS (Marie-Strumpell) (R. F. absent)
3. REITER'S DISEASE
4. GONOCCAL ARTHRITIS
5. GOUTY UVEITIS

Reiter's disease and gonococcal arthritis are both associated with anterior uveitis, migratory polyarthritis and urethritis. It is practically impossible at time to differentiate the two I do not think gouty uveitis exists as an entity. Dr. Gurman, one of our great authorities on gout, tells me he has seen over four hundred patients with gout, and states that he has never seen one with uveitis. It so happens that I have a patient who has gout and also uveitis, but I think they are unrelated.

TABLE VI

SARCOID

OCULAR FINDINGS.
- Gradual onset—usually bilateral
- Iris nodules
- Rapid formation synechiae
- Lardaceous K.P.'s
- Slow convection current, large cells
- Periphlebitis retinae
  - Cuffing, Sheathing, Tortuosity,
  - Segmented, Engorged veins
  - Tallow spots

SYSTEMIC MANIFESTATIONS:
- Lymphadenopathy, Skin eruptions
- Hepatosplenomegaly, Bone lesions

differential diagnosis is made by the dye test. if it is positive, more than likely we are dealing with toxoplasmosis. If the test is negative we should start looking for inclusion bodies, present in the urine They can be cultivated by the usual urological technics. A complement fixation test is also available.

Tropical diseases in themselves are not too common in this country, although I would like to point out that in terms of our present day population migration, we are becoming more exposed. Certainly New York City, with its large Puerto Rican and Caribbean influx, has made us entertain these diagnoses more frequently Also, with the jet age, I think we can expect to see more tropical diseases. For example, a patient with leprosy walked into the clinic for a routine check He had a phthisical left eye and an active uveitis in the right eye. We cultured leprosy bacilli from the nose He has the ears, the eyebrows, absence of the terminal phalanges, and the general leonine facies of leprosy

In regard to psychosomatic factors, some investigators, like Schlaegel, consider this to be an important factor in uveitis although others have not been so impressed

Now I wish to discuss the diagnostic procedures to be employed in uveitis This is a thorny question because all too often the clinician, confused by the absence of anything concrete in trying to make a specific diagnosis, puts the patient through a considerable workup This gives him a certain sense of accomplishment and also makes the patient feel that something is being done for him Five years ago when we started diagnostic surveys at Bellevue Hospital I had no intention of condemning this procedure; I wanted to give it a fair trial I felt that the diagnostic approach in uveitis should be dictated by the ocular history. I think the history and the ocular examination are most important and in a few instances the diagnosis can be made without any further tests. If a patient comes in with herpes zoster or a history of a recent exanthemata, the diagnosis is made. Unfortunately, these instances are all too few I would suggest doing specific tests only when one suspects a specific disease. I think that putting every patient through the same diagnostic workup is expensive, time consuming, unrewarding, and poor medicine. It shows a lack of clinical judgment, I believe, to put every patient through the same battery of identical tests We have not found that foci of infection are too important, as I mentioned before. In a series of ninety-four patients, we found only nine who had ENT pathology. Four of these had surgery for their foci but the uveitis was unimproved I think that the abuse of the patient with time consuming tests is all too common. The sedimentation rate, while frequently elevated, does not aid in making the diagnosis. Blood counts, urinalysis, and brucella agglutination tests in our hands have been very unsatisfactory. These tests, we feel, are not indicated

We think some tests are valuable when a specific disease is suspected Illustrations are the albumin-globulin ratio and the total protein and serum calcium evaluations, when sarcoidosis is suspected. In rheumatoid arthritis, the finding of a positive latex fixation test can be of help if this diagnosis is suspected The dye test in toxoplasmosis, and x-rays in tuberculosis, in sarcoid and in ankylosing spondylitis, are of value and we feel are indicated when these diseases are suspected on clinical grounds. Insofar as the

2. HERPETIC LESIONS
   a. Zoster
   b. Simplex
3. POSSIBLE VIRAL ETIOLOGY
   a. Behcet's disease
   b. Sympathetic ophthalmia
   c. Uveo-Meningeal Syndromes
      Vogt-Koyanagi
      Harada
      Sympathetic Ophthalmia?
4. CYTOMEGALIC INCLUSION DISEASE

We have found in questioning our patients that the most constant factor in those with anterior uveitis is a history of an antecedent upper respiratory infection. Since upper respiratory infections are often viral in nature, I feel that it belongs in this category. The appearance of uveitis late in the development of influenza, measles, chicken pox, or any of the exanthemata, mumps, and more rarely, hepatitis indicates a possible viral etiology. Influenza is a good example; ten days after contracting influenza a mild transient uveitis appears I feel that perhaps these are viral uveitides secondary to hypersensitivity Initially they were sensitized by a circulating viremia in the early stages of the disease and then later the eye reacted allergically. Herpetic lesions can cause uveitis although more properly it should be called a kerato-uveitis since the uveitis is frequently related to the coexisting keratitis I believe that occasionally in herpes simplex of the cornea the virus becomes fixed in the uveal tissues. I have two patients with herpes simplex of the cornea, initially associated with uveitis, who cleared completely and who now develop recurrent bouts of anterior uveitis without corneal involvement. I think that somewhere down the line the virus has become fixed in their uveal tissues and gives rise to this condition.

Behcet's disease, also known as the triple symptom complex, consists of hypopyon, uveitis and aphthous ulcers of the mucous membrane of the genitalia and of the mouth This is a recurrent disease with attacks which come on every two to three weeks With each attack there is a decrease in vision. Eventually, Behcet's disease burns itself out, usually in fifteen to twenty years. During the uveitis attacks the vision will go from 20/20 to 20/200 in three or four days; and three or four days later it will be back to 20/20 Recovery is usually good in initial attacks. It is a disease in which blindness occurs through disorganization of the anterior segment of the globe, through synechiae formation, secondary glaucoma and eventual phthisis bulbi. Blindness can also result from changes in the optic nerve

Cytomegalic inclusion disease can also cause uveitis. This is a relatively new entity occurring in children, and due to a virus It is a salivary gland inclusion virus and results in an acute uveitis which appears in new-born and very young children. It differs from toxoplasmosis in that in toxoplasmosis lesions tend to be central whereas in cytomegalic inclusion disease the lesions tend to be in the periphery. Both may present with similar clinical findings, such as splenomegaly, jaundice, thrombocytopenia, cerebral calcifications, etc. The

TABLE IX

CONTRAINDICATIONS TO THE USE OF STEROIDS

UVEITIS:
- When due to intraocular infection
  - Toxoplasmosis
  - Tuberculosis
  - Fungi
- Administer specific chemotherapy concomitantly

INFECTION:
- Corneal infections due to.
  - Fungi
  - Herpes simplex
  - Pseudomonas

INCREASED TENSION·
- Occasionally causes secondary glaucoma

SYSTEMIC DISEASES
- Tuberculosis
- Peptic ulcer
- Diabetes
- Mental depression
- Acute infectious processes

The indication for steroids, I think, is any form of anterior uveitis. Local and systemic steroids act by depressing the antigen-antibody reaction and by reducing the inflammatory reaction. In the posterior variety, I feel a steroid should be used only when there is involvement of the disk or the macula by the inflammatory process In these situations it should be given with caution Whenever possible, specific chemotherapy should be administered to cover the possible effects of steroids We have seen patients develop new satellite lesions while on systemic steroid therapy. For this reason we like to confine treatment with systemic steroids in posterior lesions to a marked allergic response, involvement of the disk, and encroachment upon the macula, by the disease process

What steroid is best for systemic administration? There is such a host of them marketed under different trade names that it is difficult to keep track of them. While the manufacturers all claim the absence of toxic side effects, because of lowered dosage, it is important to remember that while they all require different dosage schedules, the side effects are really very much the same. It is simply a matter of giving a smaller quantity of a more potent drug. If, instead of giving 300 mgs. of cortisone, one gives 0.75 mg. of decadron, it still has the same physiological effect as 300 mg. of cortisone, although it may cut down on some of the side reactions. I think that all anterior uveitides should be treated locally, and then if they don't respond it is time to use systemic steroids such as 40 mgs. of prednisolone or its equivalent, in divided doses I have rarely felt the need of using ACTH. Only occasionally have we had a better response to ACTH than to prednisolone.

One of the factors which has changed our treatment of uveitis considerably is a repository form of steroid called Depo-Medrol. We have been using it in the treatment of a wide variety of inflammatory conditions of the anterior segment. We are using it for all of our

streptococcus is concerned, our studies of the antistreptolysin titers have failed to show that this is an important cause of anterior uveitis.

Our diagnoses in a series of ninety-four patients could have been made without any laboratory aids. In other words, clinical acumen is enough in most instances. Therefore, we feel that an expensive workup is unwarranted and unnecessary. As a matter of fact, I might paraphrase a sage who stated that the amount of thinking involved in studying a patient is inversely proportional to the amount of laboratory work that is ordered; I think that is true.

TABLE VIII

TREATMENT

NON-SPECIFIC
- General measures
- Local measures
- Non-specific drugs and chemicals
- Fever therapy
- Steroids

SPECIFIC THERAPY
- Against actual cause of Uveitis if known:
  - Tuberculosis
  - Toxoplasmosis
  - Syphilis
  - Onchocerciasis

Treatment comes under the two main headings of nonspecific measures and specific therapy. Under non-specific *general measures are rest, diet, etc.* Local non-specific measures include heat, compresses, mydriatics and steroids General non-specific measures include steroids, chemicals and fever therapy. Specific therapy is directed at a specific organism *if it can be identified* Unfortunately, in uveitis we deal pretty much with the non-specific in most instances. Even if we do recognize specific conditions such as rheumatoid arthritis or sarcoid, we still do not have any specific therapy for these diseases.

Paracentesis is useful in certain instances. I have seen patients who, despite diamox and steroids, maintain elevated tension In these patients, if tension *remains* elevated for four or five days, we do a paracentesis. We do these as an out-patient procedure in the clinic and in the office. Radiation therapy is of no benefit. Mydriatics put the eye *at rest and rupture synechiae. Of all* non-specific local measures, steroids are *undoubtedly the most effective.*

Certain non-specific drugs and chemicals are used as well. Salicylates still have a role, now and then we see patients who cannot take steroids for various reasons, and they occasionally respond to large doses of salicylates. Butazolidin is a very dangerous compound to use and can cause severe kidney disease In Europe it is used a great deal. We have used it for three or four patients who responded very well I do not believe that trypsin has any value. Antibiotics should be used only for a specific purpose in specific diseases.

Now we come to steroids. I do not want to dwell too much on steroids for I think everyone here is as well acquainted with them as I am. However, certain contraindications exist to steroids, as shown in this table.

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spasm, and scopolamine relaxes their accommodation and makes them much more comfortable I think that all we need do is to treat the primary attack If it doesn't get better, give them systemic steroids They do not need a foci of infection study. We are now treating all of our acute cases with Depo-Medrol; we give them scopolamine and one subconjunctival injection of Depo-Medrol; that holds them fine.

In administering systemic steroids over a long period of time, we must watch for tension changes In chronic anterior uveitis I would like to bring out just one point; as a result of repeated attacks the blood-aqueous barrier in the ciliary body becomes damaged and allows the passage of a certain number of large molecules, proteins which ordinarily would not be found in the anterior chamber We have many patients who have flares but this is not something which requires treatment; this flare is their natural state So when I see a flare in a patient who I know has had many bouts of uveitis, I don't even treat it, I just have them come in every three months and take a look at them These patients may develop an acute attack superimposed upon this chronic flare, but otherwise it is just a chronic flare. It is like a man who has a healed broken leg; he is fine but he limps.

In posterior uveitis, I think that we should be a little cautious about giving steroids. If you suspect the presence of tuberculosis or toxoplasmosis, cover the patient with chemotherapy. This is an important thing to do Use steroids only if there is involvement of the macula or the papilla If there is a focus on the periphery, I don't treat the patient; I don't give him steroids I am accumulating a very impressive series of patients who do very well and recover spontaneously with no treatment at all.

So, in conclusion, I would like to say that classification is still in doubt; I think an anatomical classification still is the best one which we have today. Pathogenesis still has to be worked out although I think the hypersensitivity mechanism probably is the most important and most logical one in the causation of uveitis. Diagnostic surveys in our experience are not too helpful, as I have said Therapy, I believe, is still largely non-specific and we have to rely largely upon steroids

acute uveitides. We give ½ c.c. (20 mg.) as a subconjunctival injection in the upper outer quadrant, and we find that this has an effectiveness of from seven days to three weeks. Many uveitis patients with moon facies, due to long term use of systemic steroids, have been controlled with Depo-Medrol used in this way. The repository form is absorbed very slowly for a period of from two to three weeks and it is often so effective that systemic steroids are not required. We have many non-English-speaking patients who find it difficult to understand our instructions, nor can we rely upon their taking their medication as prescribed. By injecting Depo-Medrol, however, we know the patient is getting the proper medication In many instances, if a patient cannot take systemic steroids, we advocate the use of Depo-Medrol. It gives a high concentration locally, without any systemic effects, and it lasts for some time

In the treatment of sarcoid, dilation of the pupils is most important since synechiae form so rapidly, and there is very little we can do about it if they do form. On the other hand, I think it is a good idea to gonioscope these patients regularly because many of them have narrow angles and we want to make sure we are not crowding the iris into the angle, thus causing a rim of peripheral anterior synechiae. We are between the devil and the deep blue sea I think sarcoid patients should take systemic steroids or conjunctival Depo-Medrol immediately. I don't believe topical steroids are enough to carry them through the acute phase; they must be watched closely and have frequent gonioscopic examinations.

The treatment of sympathetic ophthalmia is quite obvious; if it is an irritable fluid eye, enucleate it at once and halt all worry on that score. But if you believe the eye will have any useful function, I think it should be spared, and with ACTH and steroids there is much greater opportunity to save the eye. As a matter of fact, we have had about four patients with sympathetic ophthalmia and only one of them needed ACTH.

In viral diseases, such as herpes zoster, Scheie claims he gets good results with ACTH. I think any kind of systemic steroid is adequate and that ACTH does no more than a systemic steroid. In herpes simplex, of course, you must not use steroids. In Behcet's disease, even though the literature says steroids are not indicated, I must say that the only thing that has helped my patients with this disease is the steroids which they have been receiving. In rheumatic diseases, there is no specific agent that we know of which causes these diseases, so there again we go back to non-specific methods. Maybe the internist is already treating the rheumatic patient with steroids, and frequently this will ameliorate the uveitis a bit, so that all we need do is to give him local treatment. However, if the patient develops band shaped calcification of the cornea, I think the vision can be improved by the use of sodium versenate to chelate away the calcium This has a remarkable effect, the calcium just disapepars. Ankylosing spondylitis is best treated with steroids. Most treatment of uveitis must be non-specific, since, unfortunately, the etiology often is not clear.

In resumé, in anterior uveitis give the patients local medication, such as any one of the drop forms of hydrocortisone, and dilate them with scopolamine. Once they are dilated, you don't have to worry about them anymore if they are on steroids. They have a great deal of ciliary

EDITOR'S COLUMN

KENNETH L. CRAFT, M. D.

Indianapolis, Indiana

This is Volume 1, Number 1, of the Transactions of the American Society of Ophthalmologic and Otolaryngologic Allergy. The recommendation of the Council for the establishment of this magazine was due to several reasons. In recent years there has been a growing dissatisfaction with the time at which the annual meeting was held and an increasing demand by the membership at large that the Society return to its original meeting time, i.e., upon the day immediately preceding the convention of the American Academy of Ophthalmology and Otolaryngology. Several years ago, as an inducement to persuade our Allergy Society to hold its meeting on the last day of the Academy week, the Academy offered to publish the scientific papers of the Allergy Society program in the Transactions of the American Academy. In changing back to its original time of meeting, our Society could not expect this arrangement to continue. Also, there were business matters and other important items of interest which did not reach the Society members through the medium of the Academy Transactions. In addition, it usually was many months, often more than a whole year, after the meeting before our program papers were published. Another important factor was that many of the Allergy Society members do not belong to the American Academy and thus do not receive its publications.

And so was born the Transactions of the American Society of Ophthalmologic and Otolaryngologic Allergy. We hope you like it. We hope that you will let us know what you think of it and if you approve of the general idea of an official publication for the Society. We are aware of the inadequacies of this first edition and we hope that you will help us improve future issues by sending in your suggestions and constructive criticism. Would you like to see other features added, and if so, what? Please give us your honest opinions; we like sweet smelling bouquets but for this purpose we prefer the real low-down. So don't hold your punches.

A feature of the 1960 meeting was the Instructional Course, a new departure in our annual meetings. Excerpts from the experts at the eight Conference Tables may be found on other pages of this volume. This part of the program proved so popular that there have been many requests that the Instructional Course be repeated in 1961. Plans already are under way to enlarge this phase of the general program by adding more instructors and more subjects and by allotting more time for the presentation of these courses. What subjects would YOU like to hear discussed?

The general approval of the changes made in the time of holding the meeting and in the type of program presented was indicated by the large attendance at the Chicago meeting. The total registration of members and guests was the largest of recent years.

The facilities of the Sherman Hotel proved to be adequate in every respect for the meeting and for the annual ban-

PRESIDENT'S PAGE

LELAND H. PREWITT, M. D.

Ottumwa, Iowa



The American Society of Ophthalmologic and Otolaryngologic Allergy most cordially invites its members and the members of the American Academy of Ophthalmology and Otolaryngology to attend the twenty-first meeting of the Society at the Sherman Hotel in Chicago on Saturday, October 7, 1961. Our endeavor to cooperate with the Academy by changing our meeting time from Saturdays prior to the Academy to Friday at the conclusion of the meeting, ended in complete failure after several years' trial. Numerous attempts to get an evening earlier in the week were unsuccessful. Lack of time because of the numerous meetings available today, and complete mental saturation and fatigue, forced the change back to our original pre-convention Saturday date.

To satisfy a long desired need for the ophthalmologist and otolaryngologist to recognize and treat the many allergic phenomena that occur in everyday practice, the American Society of Ophthalmologic and Otolaryngologic Allergy has arranged to give a series of round table instructional courses in the morning program. Various allergy subjects with two instructors at each table will be arranged, where personal problems, new information, lab techniques, and treatment will be discussed. Our desire is to make these courses so practical that you can return home and practice modern, up-to-date allergic otolaryngology and ophthalmology. Coffee breaks will give you a chance to renew old friendships and make new contacts.

The afternoon will be devoted to papers of practical and scientific interest presented by the best qualified speakers on such subjects as repository therapy, enzymatic therapy, ocular allergy and psychosomatic allergy If you wish a particular subject discussed, kindly send in your request.

Make your reservations now, tell your friends, invite the interns and younger men and let's make this year's meeting one of the most profitable and entertaining we have had to date. Allergy is on the move, let's keep up with it and its modern concepts by attending and taking an active part in the meeting. You are most cordially welcome.

BUSINESS SESSION

The annual business meeting was called to order by President Walter E. Owen

Dr. Owen announced that since the minutes of the last regular meeting had been sent to each member of the Society, it would not be necessary to read these minutes at the present meeting It was moved and passed that the minutes of the last meeting (1959), containing also the Treasurer's report, be accepted as published in the Secretary-Treasurer's recent letter to the membership

REPORT OF COUNCIL

Dr Sam H. Sanders, speaking for the Council, reported that the following matters pertaining to the welfare of the Society had been carefully considered at the meeting of the Council, held on October 7, 1960, and had been recommended for adoption and passage by the Society

(1) An amendment to the By-Laws covering a proposed new type of membership to be added to the present membership classification, was recommended. The new classification shall be known as Life Members and shall consist of those members of the Society who have retired from the practice of medicine or who have been members of the Society in good standing for a period of twenty-five years, and who shall apply to the Council for transfer to the Life Member classification. Life Members shall have the privilege of participating in all meetings and activities of the Society and shall not be required to pay dues, but may not hold office nor have voting privileges They shall *not* receive the Bulletin or any official publication of the Society, except by payment of the subscription fee set by the Council. The classification of Life Member shall be bestowed by vote of the Society upon recommendation by the Council.

(2) It was recommended that a letter be written by the Society Secretary to the American Medical Association, with a copy to the Secretary of the American Otorhinologic Society for Plastic Surgery, such letter to state that the American Society of Ophthalmologic and Otolaryngologic Allergy disapproves of the undesirable publicity practices of the American Board of Plastic Surgery which has sponsored certain misleading articles appearing in some lay magazines in regard to qualifications for the practice of plastic surgery.

(3) The Council recommended that the proceedings of the annual meetings of the Society be published in a magazine to be known as the Transactions of the American Society of Ophthalmologic and Otolaryngologic Allergy, and that a copy be sent to each member. It was further recommended that Dr. Kenneth L. Craft, of Indianapolis, be appointed as Editor of the Transactions.

(4) It was recommended that Doctors De Stio and Craft be appointed as a committee to arrange for the manufacture of a distinctive plaque to be presented to the Past-Presidents of the Society, and to each President upon his retirement from office. (This plaque is to take the place of the cuff links which currently are presented to each President at the end of his term of office.)

(5) The Council recommended that the Secretary of the Society notify the proper officials of the American Acad-

quet. This party was held in the attractive Skyline Terrace Room where the view of the city, with its skyline and beautiful Lake Michigan in the background, reminds one of the Top o' the Mark in San Francisco. An excellent dinner was preceded by a lavish cocktail party furnished through the courtesy of Spencer Laboratories and Wampole Laboratories, in collaboration as hosts. Arrangements have already been made to return to the Sherman for the 1961 meeting, which will be held on Saturday, October 7. Plan now to attend.

Please note the advertisements appearing in this magazine. Much of the expense of the publication of the Transactions thus is underwritten by these firms. Let us express our appreciation of this support by giving the detail men representing these companies a warm welcome, at least, when they come calling.

A vote of thanks and a tip o' the hat to Rovin' Joe Hampsey, the official photographer at the 1960 meeting. Joe not only helped moderate one of the Table Conferences but also circulated about the other Tables, taking pictures for the Transactions instead of harvesting the fast dropping pearls.

COMMITTEES FOR 1961

The following committee appointments have been announced by President Prewitt.

Program

Section on Otolaryngology

French K Hansel, Chairman
Linden J. Wallner
Herbert P. Harkins
Sylvester C Missal

Section on Ophthalmology

Leland H Prewitt, Chairman
Frederick H. Theodore
Robert S Coles

Instructional Course

Kenneth L Craft, Chairman
Walter E Owen
Sam H Sanders

Publicity

Sam H Sanders, Chairman
Jack R Anderson
Glenn J. Greenwood
Walter T. Hotchkiss

Nominating

Kenneth L. Craft, Chairman
Bernard M. Barrett
William H Evans
Herbert P Harkins

Auditing

Joseph W. Hampsey, Chairman
William P. Hofmann
George N. Jewell
George W. Ryall

Liaison

Victor R. Alfaro, Chairman
Edward W. Harris
Edley H Jones
L. Q. Pang

Entertainment

Bernard M. Barrett, Chairman
Michael H. Barone
Kelvin A. Kasper
Lawrence S. Crispell

emy of Ophthalmology and Otolaryngology that the American Society of Ophthalmologic and Otolaryngologic Allergy strongly recommends that more instruction courses in Allergy and Medical Otolaryngology and Ophthalmology be offered to the members of the Academy.

(6) Applicants for membership in the Society were *recommended for election* as follows:

FELLOWS

Barratt, Wm. E., M. D., 30 South Park Place, Painesville, Ohio

Bruce, Robert G., M. D, 8130 Santa Clara Drive, Dallas 18, Texas

Coles, Robert S, M D, 125 East 72nd Street, New York, N. Y.

Draper, W Leonard, M. D., 540 Herman Professional Bldg, Houston 25, Texas

Droege, Fred D, M D., 207 Medical Arts Bldg., Sarasota, Florida

Guibor, George P., M. D, 25 East Washington Street, Chicago 2, Illinois

Kuhn, Arthur J, M. D, 112 Rimbach Street, Hammond, Indiana

Maher, Joseph J, M D, 30 South Park Place, Painesville, Ohio

Olson, Burton G, M D., McCannal Clinic, Minot, North Dakota

Warren, Claude M., Jr., M D, 1720 Springhill Avenue, Mobile, Alabama

Witchell, Ira S, M D, 2021 Grand Concourse, Bronx 53, New York

ASSOCIATES

Chew, William, M. D., 1027 West Main Street, Leesburg, Virginia

Higgins, Eugene W., M. D., 3433 Wisconsin Avenue, N. W, Washington, D. C.

(7) The Council recommended the election of the following officers to serve for the coming fiscal year:

President.....Leland H. Prewitt, M. D.
Ottumwa, Iowa
President-Elect..Edley H Jones, M. D.
Vicksburg, Mississippi
Vice-President................
... .Lawrence S Crispell, M. D.
Joplin, Missouri
Secretary-Treasurer...........
...........Daniel S. De Stio, M. D.
Pittsburgh, Pennsylvania

(8) The Council recommended the election of the following Council members to serve for a period of three years:

Michael H. Barone, M D., Buffalo, New York

Kenneth L. Craft, M. D., Indianapolis, Indiana

Linden J. Wallner, M D, Chicago, Illinois

The above recommendations made by the Council were adopted by vote of the members present at the annual business meeting.

President Owen presented the gavel of office to incoming President Leland H Prewitt who congratulated Dr. Owen upon the success of his year's administration, culminating in the present meeting. Dr. Prewitt appealed to the membership *for help and suggestions relative* to the program for next year's meeting, and closed his talk by calling attention to the great potential influence possessed by this Society in promoting further study and research in the field of ophthalmologic and otolaryngologic allergy.

ADJOURNMENT

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Ottumwa, Iowa

President-Elect..Edley H. Jones, M. D.
Vicksburg, Mississippi

Vice-President.................
........Lawrence S. Crispell, M. D.
Joplin, Missouri

Secretary-Treasurer...........
...........Daniel S. De Stio, M. D.
Pittsburgh, Pennsylvania

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ADJOURNMENT

Clarysse, J. M., Bruges, Belgium
Fitch, Frank W., Chicago, Ill.
Greiner, W. R., Seattle, Wash
Halpin, Lawrence J., Cedar Rapids, Iowa
Klestad, W. D., Fall River, Mass
McMahon, B T., Denver, Colo.
Moffitt, Dwight D, Philadelphia, Pa.
Powers, W. H., Oak Park, Ill.
Tyson, J. M., DuBois, Pa
Walker, Jack, Sandusky, Ohio
Walker, James E., Sandusky, Ohio
Webb, James J., Blytheville, Ark

Your name should be in this list in 1961.

TIME—Saturday, October 7.
PLACE—Sherman Hotel, Chicago, Ill
OCCASION—Annual meeting of the American Society of Ophthalmologic and Otolaryngologic Allergy.

PLAN NOW TO BE THERE

REGISTRATION AT CHICAGO

Following is a list of those who attended the 1960 meeting at the Sherman Hotel:

MEMBERS

Alfaro, Victor R., Washington, D. C.
Anderson, Edwin R., Warren, Pa.
Barone, Michael H., Buffalo, N. Y.
Barnet, E. G., Phoenix, Ariz.
Barrett, Bernard M., Pensacola, Fla.
Barry, William H., Kansas City, Mo.
Baxter, Edward J., Sandusky, Ohio
Bergin, Joseph H., Alma, Mich.
Brickley, Daniel W., Jr., Marion, Ohio
Brown, Charles W., San Diego, Calif.
Brown, Samuel P., Moline, Illinois
Budetti, Joseph A., Wichita, Kansas
Clements, Ralph M., Tuscaloosa, Ala.
Craft, Kenneth L., Indianapolis, Ind
Crispell, Lawrence S., Joplin, Mo.
Coles, Robert S., New York, N. Y.
Cruthirds, Archie E., Phoenix, Ariz.
Davol, Rector T., Greenwich, Conn.
De Stio, Daniel S., Pittsburgh, Pa.
Dolowitz, David A., Salt Lake City, Utah
Donnell, Herbert, Waxahachie, Texas
Droege, Fred D., Sarasota, Fla.
Duboe, Sidney H., Los Angeles, Calif.
Evans, William H., Youngstown, Ohio
Flatley, Robert E., Moline, Ill.
Gerston, John, Columbus, Ohio
Gill, Earl K., Corpus Christie, Texas
Goldman, Herbert B., Rockville Centre, N. Y.
Gomillion, Jesse D., Midland, Texas
Griesman, Bruno L., New York, N. Y.
Hall, Albert W., Berwyn, Ill.
Hansel, French K., St. Louis, Mo.
Harkins, Herbert P., Philadelphia, Pa.
Hampsey, Joseph W., Pittsburgh, Pa.
Heetderks, Dewey R., Grand Rapids, Mich.
Hill, Howard E., Muncie, Ind.
Higgins, Eugene W., Washington, D. C.
Hitch, Donald A., Hamilton, Ontario, Canada
Hope-Gill, Donald, Niagara Falls, Ontario, Canada
Hopkins, Julius H., Petersburg, Va
Jewell, George M., Kokomo, Ind.
Jones, Edley H., Vicksburg, Miss.
Kudolla, Charles R., Casper, Wyo.
Layton, Rex G., Lewistown, Idaho
Loomis, George L., Winona, Minn.
Lownik, Felix J., Freeport, Ill.
McComiskey, Arthur J., New Orleans, La.
Mazique, Douglas W., Chicago, Ill.
Missal, S. C., Cleveland, Ohio
O'Toole, Francis A., Clinton, Mass.
Owen, Walter E., Peoria, Ill.
Owsley, Guy A., Hartford City, Ind.
Prewitt, Leland H., Ottumwa, Iowa
Raffaele, Frank J., New York, N. Y.
Randolph, Theron, Chicago, Ill.
Ringer, A. L., Springfield, Ohio
Ross, Ervin S., Cincinnati, Ohio
Ruddy, Lorenz W., Sacramento, Calif.
Ryall, George W., Shaker Heights, Ohio
Sanders, Sam H., Memphis, Tenn.
Schoetker, George H., Clearwater, Fla.
Smith, Thomas L., Lorain, Ohio
Smith, Thomas T., Omaha, Neb.
Sorenson, Elmer M., Red Oak, Iowa
Stahl, Richard H., Cuyahoga Falls, Ohio
Thel, Henry C. Aliquippa, Pa.
Trunzo, Thomas H , Latrobe, Pa.
Wallace, Thomas H , Clearwater, Fla.
Wallner, Linden J , Chicago, Ill.
Warren, Claude M., Mobile, Ala.
Welton, W. D., Jr., Dayton, Ohio

GUESTS

Allison, A. M., Alice, Texas
Christensen, E., Lexington, Ky.

Claysse, J. M., Bruges, Belgium
Fitch, Frank W., Chicago, Ill.
Greiner, W. R., Seattle, Wash
Halpin, Lawrence J., Cedar Rapids, Iowa
Klestad, W. D., Fall River, Mass
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